



**INFORMATION FOR GENERAL PRACTITIONERS
ABOUT THE BREAST CANCER DRUG**

Trastuzumab (Herceptin®)



In April 2007 the National Breast Cancer Centre published a new clinical practice guideline about the use of trastuzumab (Herceptin®) for the treatment of breast cancer. The guideline was developed by a multidisciplinary working group and summarises the best available international evidence, including research published up to November 2006. The guideline is intended for use by health professionals involved in the management of patients with early and advanced breast cancer. The following summary provides information that may be helpful for general practitioners in answering patient's questions about trastuzumab.

RECOMMENDATIONS

The guideline recommends that:

- trastuzumab (Herceptin®) should be offered with chemotherapy after surgery for patients with HER2-positive early breast cancer
- women receiving trastuzumab (Herceptin®) should be monitored for signs of cardiac dysfunction* every three months
- trastuzumab (Herceptin®) should be offered with chemotherapy as first-line treatment for patients with HER2-positive metastatic breast cancer
- trastuzumab (Herceptin®) can also be offered alone to patients with HER2-positive metastatic breast cancer who have already received chemotherapy or in patients for whom chemotherapy is not appropriate.

Trastuzumab is not recommended for people who have a prior history of significant cardiac dysfunction* and should not be given to patients receiving concurrent anthracycline chemotherapy (epirubicin, doxorubicin, adriamycin).

**including documented congestive heart failure, coronary artery disease with previous Q-wave myocardial infarction, angina pectoris requiring medication, uncontrolled hypertension, clinically significant valvular disease, or unstable arrhythmias.*

WHAT IS TRASTUZUMAB (HERCEPTIN®)?

Trastuzumab (Herceptin®) is a targeted therapy for the treatment of breast cancer. Trastuzumab targets a type of breast cancer called HER2-positive breast cancer. 'HER2-positive' means that the breast cancer cells express high levels of the HER2 protein on their surface. About one in five patients diagnosed with breast cancer have HER2-positive breast cancer – a more aggressive form of the disease. If breast cancer cells are not HER2-positive, trastuzumab will have no benefit.

MEASUREMENT OF HER2 STATUS

Assessment of HER2 status is performed on samples obtained by core or surgical biopsy. Three tests can be done to determine whether a breast cancer is HER2-positive:

- FISH (fluorescence in-situ hybridisation)
- CISH (chromogenic in-situ hybridisation)
- IHC (immunohistochemistry).

Eligibility for trastuzumab (Herceptin®) on the Pharmaceutical Benefits Scheme for patients with early breast cancer is dependent on a positive ISH (FISH or CISH) test. Eligibility for trastuzumab (Herceptin®) by patients with metastatic breast cancer is dependant on an IHC score of 3+ or a positive ISH test (FISH or CISH). For patients with an IHC score of 2+, subsequent confirmation by ISH is required. Pathology testing should be ordered by the surgeon who performed the patient's biopsy.

POTENTIAL BENEFITS OF TRASTUZUMAB (HERCEPTIN®) FOR PATIENTS WITH BREAST CANCER

Early breast cancer

Treatment with trastuzumab (Herceptin®) significantly reduces the risk of breast cancer recurring and reduces the risk of death for women with HER2-positive early breast cancer.

Clinical trials showed that trastuzumab therapy reduced the risk of breast cancer coming back in women with early breast cancer by between 5% and 13%; the relative risk of recurrence was reduced by 52%.

A 33% increase in overall survival was reported among women receiving trastuzumab and chemotherapy. The absolute difference in the number of deaths between women receiving trastuzumab and chemotherapy and women receiving chemotherapy alone was between 1% and 7%.

Metastatic breast cancer

Treatment with trastuzumab (Herceptin®) can decrease the size of secondary breast cancer lesions and improves the survival for patients with HER2-positive metastatic breast cancer.

Clinical trials showed that women treated with trastuzumab reduced their risk of cancer progressing by 5%. Women treated with trastuzumab and chemotherapy lived longer than women treatment with chemotherapy alone. One trial found a median survival increase of 4.8 months; another reported a median survival increase of 8.5 months.

ADMINISTRATION OF TRASTUZUMAB (HERCEPTIN®)

Trastuzumab is given by slow intravenous (IV) infusion. The infusion is given either weekly (a loading dose of 4mg/kg then 2mg/kg) or 3-weekly (a loading dose of 8mg/kg then 6 mg/kg). The first infusion usually takes 90 minutes and can be slowed or stopped if the patient experiences discomfort. If the patient has no reaction to the first infusion, subsequent infusions will be quicker – about 30 minutes.

DURATION OF TRASTUZUMAB (HERCEPTIN®) TREATMENT

For patients with early breast cancer, trastuzumab (Herceptin®) therapy is recommended for 1 year. Clinical trials are examining whether trastuzumab is more effective if given for 2 years and whether trastuzumab is as effective if given for a shorter period of time. One small clinical trial suggested that similar benefits were obtained from nine-weekly treatments. This suggests that for patients who are unable to complete a full year of therapy due to cardiotoxicity or other reasons, some benefit may still be derived from a shorter duration of treatment.

For patients with metastatic breast cancer trastuzumab (Herceptin®) therapy should be continued for as long as an individual is gaining benefit from treatment and the benefits outweigh the risks and side effects.

POTENTIAL SIDE EFFECTS OF TRASTUZUMAB (HERCEPTIN®)

The most significant side effect of trastuzumab (Herceptin®) is the risk of cardiac dysfunction. The risk of cardiac dysfunction is increased if trastuzumab is given in combination with certain types of chemotherapy.

Trastuzumab is not recommended for people who have a prior history of cardiac dysfunction and should not be given together with anthracycline chemotherapy (epirubicin, doxorubicin, adriamycin).

Patients on trastuzumab therapy should be monitored every 3 months for symptoms or clinical signs of congestive heart failure, coronary artery disease or angina, hypertension, valvular disease or cardiac arrhythmias. Cardiac function must be tested by a suitable method including, for example, ECHO or MUGA, at 3-monthly intervals during treatment. Testing is usually arranged by the patient's oncologist. If symptoms or clinical signs of cardiac dysfunction are detected at any time, the patient's oncologist should be consulted.

In clinical trials, infusion reactions such as chills, fever, nausea

and vomiting occurred in nearly half of all women receiving trastuzumab. These side effects usually occurred during and shortly after treatment. These symptoms can be controlled or reduced by medication. Other side-effects, including lung problems, occurred infrequently with subsequent infusions. Trials in metastatic breast cancer have also reported anaemia, leukopenia and neutropenia in women receiving trastuzumab and chemotherapy.

UNANSWERED QUESTIONS ABOUT TRASTUZUMAB

A number of questions remain unanswered about the use of trastuzumab in early and metastatic breast cancer, including:

- optimal duration of adjuvant trastuzumab with chemotherapy
- optimal sequence/timing of adjuvant trastuzumab with chemotherapy
- continued use of trastuzumab post-progression in patients with metastatic breast cancer
- use of trastuzumab as a single agent
- use of trastuzumab in locally advanced and inflammatory breast cancer
- long-term benefits and adverse effects of trastuzumab, including side effects when given with radiotherapy
- use of trastuzumab in pregnancy, and impact on fertility and contraception.

PHARMACEUTICAL BENEFITS SCHEME LISTING FOR TRASTUZUMAB (HERCEPTIN®) AS OF NOVEMBER 2006

Herceptin® (trastuzumab) is currently subsidised for the treatment of HER2-positive patients with early breast cancer concurrently with chemotherapy following surgery; restrictions apply.

Herceptin® (trastuzumab) is currently subsidised for the treatment of HER2-positive patients with metastatic breast cancer:

- in combination with taxanes for patients who have not received chemotherapy for metastatic disease
- as monotherapy for the treatment of those patients who have received one or more chemotherapy regimens(s) for metastatic disease.

Trastuzumab is provided as a section 100 Authority required benefit. See www.medicareaustralia.gov.au/providers for further information.

ORDERING THE GUIDELINE

The guideline can be downloaded or ordered online at the National Breast Cancer Centre's website www.nbcc.org.au/resources or by calling 1800 624 973.

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