NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Trastuzumab, as monotherapy and in combination with a taxane, for the treatment of metastatic breast cancer (to include a review of TA 34)

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of trastuzumab, as monotherapy and in combination with a taxane, within its licensed indication, for the treatment of metastatic breast cancer (to include a review of TA 34).

Background

Breast cancer is the most common cancer in women, accounting for approximately 31 per cent of all newly diagnosed cases of cancer in women each year. In 2006 there were 45,822 new cases of breast cancer diagnosed in the UK. Breast cancer is the second most common cause of cancer death in women. In 2007, 11,990 women died from breast cancer in the UK. Breast cancer in men is rare, with about 260 cases diagnosed and 68 deaths in England and Wales each year. Breast cancer risk is strongly related to age, with 81% of cases occurring in women aged 50 years and over.

Metastatic (or stage IV) breast cancer describes the presence of disease at distant sites such as the bone, liver, or lung. The lymph nodes may also be affected. It has been estimated that between 16-20% of women initially presenting with breast cancer have locally advanced disease or distant metastases. Approximately 40-50% of women diagnosed with early or localised breast cancer will eventually relapse and develop metastatic breast cancer. Average life expectancy for untreated patients with metastatic breast has in the past been approximately 12 months; this increases to 18-24 months with treatment.

The role of current treatments is to palliate symptoms, prolong survival and maintain a good quality of life with minimal adverse events. The key decisions involving choice of treatment are based on previous therapy, oestrogen receptor status and the extent of the disease. The NICE clinical guideline for advanced breast cancer (CG81) recommends first-line treatment with an anthracycline-based chemotherapy regimen. Following disease progression on an anthracycline, other chemotherapy options include single-agent or combination taxanes, capecitabine, vinorelbine, lapatinib and gemcitabine. For patients with HER2 positive tumours, trastuzumab in combination with either a taxane or an aromatase inhibitor may be used depending on whether a patient is considered to require immediate chemotherapy. CG81 also recommends that for patients who are receiving treatment with trastuzumab for advanced breast cancer, treatment with trastuzumab should be

discontinued at the time of disease progression outside the central nervous system. Trastuzumab should not be discontinued if disease progression is within the central nervous system alone. NICE Technology Appraisal No. 34, March 2002, recommends the use of trastuzumab as monotherapy and in combination with paclitaxel (see appendix for details).

The technology

Trastuzumab (Herceptin, Roche) is a recombinant humanised monoclonal antibody, given intravenously, that attaches to the HER2 receptor protein on the surface of the cancer cell and affects its growth. Trastuzumab is only used in patients whose tumours have either HER2 over expression or HER2 gene amplification as determined by an accurate and validated test.

As monotherapy, trastuzumab has UK market authorisation for patients who have received at least two chemotherapy regimens for metastatic breast cancer; prior chemotherapy must have included at least an anthracycline and a taxane, unless these treatments are inappropriate; patients who are oestrogen receptor-positive must also have failed to respond to appropriate hormonal therapy.

In combination with paclitaxel, trastuzumab has UK market authorisation for patients with metastatic breast cancer who have not received chemotherapy for metastatic disease and in whom an anthracycline is unsuitable.

In 2004, the UK market authorisation was extended to include trastuzumab in combination with docetaxel for patients with metastatic breast cancer who have not received chemotherapy for metastatic disease.

Intervention(s)	Trastuzumab monotherapy Trastuzumab in combination with a taxane
Population(s)	Adults with HER2 positive metastatic breast cancer

Comparators	Trastuzumab in combination with docetaxel should be compared with trastuzumab in combination with paclitaxel. In addition trastuzumab in combination with a taxane should be compared with: • docetaxel monotherapy • paclitaxel monotherapy • gemcitabine with paclitaxel • capecitabine with docetaxel • best supportive care Trastuzumab monotherapy should be compared with: • vinorelbine • capecitabine • best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 116, Jan 2007, 'Gemcitabine for the treatment of metastatic breast cancer'. Expected review date January 2010. Technology Appraisal No.62, May 2003, 'Guidance on the use of capecitabine for the treatment of locally advanced or metastatic breast cancer '. Updated in clinical guideline 81. Technology Appraisal No.54, December 2002, 'Guidance on the use of vinorelbine for the treatment of advanced breast cancer '. Updated in clinical guideline 81. Technology Appraisal No. 34, Mar 2002, 'Guidance on the use of trastuzumab for the treatment of advanced breast cancer'. Currently subject to review. Publication date tbc. Technology Appraisal No. 30, September 2001, 'Taxanes for the treatment of breast cancer'. Updated in clinical guideline 81. Technology Appraisal in Preparation, 'Lapatinib for breast cancer (for use in women with previously treated advanced or metastatic breast cancer)'. Earliest anticipated date of publication February 2010. Technology Appraisal in Preparation, 'Sunitinib in combination with capecitabine for the treatment of advanced and/or metastatic breast cancer'. Earliest anticipated date of publication Oct 2011. Related Guidelines: Clinical Guideline No. 81, Feb 2009, 'Advanced breast cancer: diagnosis and treatment'. This guideline updates and replaces technology appraisal guidance 62 (capecitabine), 54 (vinorelbine) and 30 (taxanes).

Questions for consultation

Have the most appropriate comparators for the treatment of metastatic breast cancer been included in the scope? Are the comparators listed routinely used in clinical practice?

Should the appraisal include consideration of continuation of trastuzumab post progression, particularly if disease progression is within the central nervous system alone? If so, what should the comparators be (for example, lapatinib)?

How should best supportive care be defined, in terms of trastuzumab monotherapy and trastuzumab in combination with a taxane?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Multiple Technology Appraisal (MTA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)

Appendix: Current NICE Guidance (TA34)

1.1. Trastuzumab in combination with paclitaxel (combination trastuzumab is currently only licensed for use with paclitaxel) is recommended as an option for people with tumours expressing human epidermal growth factor receptor 2 (HER2) scored at levels of 3+ who have not received chemotherapy for metastatic breast cancer and in whom anthracycline treatment is inappropriate.

1.2. Trastuzumab monotherapy is recommended as an option for people with tumours expressing HER2 scored at levels of 3+ who have received at least two chemotherapy regimens for metastatic breast cancer. Prior chemotherapy must have included at least an anthracycline and a taxane where these treatments are appropriate. It should also have included hormonal therapy in suitable oestrogen receptor positive patients.

1.3. HER2 levels should be scored using validated immunohistochemical techniques and in accordance with published guidelines. Laboratories offering tissue sample immunocytochemical or other predictive tests for therapy response should use validated standardised assay methods and participate in and demonstrate satisfactory performance in a recognised external quality assurance scheme.