NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Pertuzumab in combination with trastuzumab and a taxane for the treatment of HER2 positive metastatic breast cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost-effectiveness of pertuzumab in combination with trastuzumab and a taxane within its licensed indication for the treatment of human epidermal growth factor receptor 2 (HER2) positive metastatic breast cancer.

Background

There were over 42,000 women and around 300 men newly diagnosed with breast cancer in England and Wales during 2008, and around 11,000 deaths.

Metastatic 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 5% of women initially presenting with breast cancer have locally advanced disease or distant metastases.

HER2 is a receptor for a particular growth factor called human epidermal growth factor, which occurs naturally in the body. When human epidermal growth factor attaches itself to HER2 receptors on breast cancer cells, it can stimulate the cells to divide and grow. Some breast cancer cells have more HER2 receptors than others. In this case, the tumour is described as being HER2-positive. It is thought that about 1 in 5 women with breast cancer will have HER2-positive tumours.

The role of current treatments for metastatic breast cancer is to palliate symptoms, prolong survival and maintain a good quality of life with minimal adverse events. Treatment depends on, oestrogen receptor status, HER2 status and the extent of the disease.

NICE clinical guideline 81 (CG81) for advanced breast cancer, which covers both first and subsequent lines of therapy, recommends first-line treatment with an anthracycline-based chemotherapy regimen. Where an anthracycline is unsuitable (for example, if the person has previously received anthracycline-based adjuvant therapy or has a contraindication to anthracyclines) docetaxel monotherapy should be considered. NICE technology appraisal No. 34 recommends trastuzumab in combination with paclitaxel as an option for people with tumours expressing HER2 scored at levels of 3+ who have not received chemotherapy for metastatic breast cancer and in whom anthracycline treatment is inappropriate. In clinical practice,

trastuzumab in combination with either paclitaxel or docetaxel may be used as first-line therapy for patients with HER2 positive tumours.

The technology

Pertuzumab (brand name unknown, Roche Products) is a monoclonal antibody targeting HER2. Pertuzumab binds to the HER2 receptor and prevents the pairing (dimerisation) of HER2 with other HER family receptors, inhibiting intracellular signalling. It is administered by intravenous infusion.

Pertuzumab does not have a UK marketing authorisation for the treatment of HER2 positive metastatic breast cancer. It has been studied in clinical trials in combination with trastuzumab and a taxane compared with trastuzumab plus a taxane without pertuzumab in adults with HER2-positive metastatic breast cancer who have not received any prior chemotherapy for their metastatic breast cancer. It has also been studied in combination with trastuzumab-emtasine compared with trastuzumab-emtasine without pertuzumab in adults with metastatic breast cancer who have not received any prior chemotherapy for their metastatic breast cancer.

Intervention(s)	Pertuzumab in combination with trastuzumab and a taxane
Population(s)	Adults with HER2-positive metastatic breast cancer who have not previously received chemotherapy or HER2 directed treatment for metastatic disease
Comparators	• Trastuzumab in combination with a taxane (docetaxel or paclitaxel) • Lapatinib in combination with paclitaxel (subject to ongoing NICE appraisal)
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. 34, March 2002, 'Trastuzumab for the treatment of advanced breast cancer'. Review suspended. Technology Appraisal No. 214, February 2011, 'Bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer' (replaces Technology Appraisal No. 147). Review date July 2013. Technology Appraisal in Preparation 'Bevacizumab in combination with capecitabine for the first line treatment of metastatic breast cancer.' Earliest anticipated date of publication August 2012. Technology Appraisal in Preparation 'Lapatinib and trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormone receptor positive breast cancer which over-expresses HER2'. Earliest anticipated date of publication TBC. Proposed Technology Appraisal 'Lapatinib in combination with paclitaxel for the first-line treatment of HER2 positive metastatic breast cancer'. Earliest anticipated date of publication TBC. Related Guidelines: Clinical Guideline No. 81, February 2009, 'Advanced breast cancer: diagnosis and treatment' (replaces previous Technology Appraisals No. 30, 54 and 62). Review date February 2012. Related Breast Cancer Pathways: http://pathways.nice.org.uk/pathways/breast-cancer

Questions for consultation

Have the most appropriate comparators for pertuzumab for the treatment of HER2 positive metastatic breast cancer been included in the scope? Are the comparators listed routinely used in clinical practice?

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

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) 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)