NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Trastuzumab emtansine for treating HER2-positive, unresectable locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of trastuzumab emtansine within its licensed indication for the treatment of unresectable locally advanced or metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane.

Background

Breast cancer is a common cancer in the UK. In 2010 there were around 44,000 new diagnoses of breast cancer and around 10,300 deaths from breast cancer in England and Wales.

Locally advanced cancers are defined as being larger than five centimetres and may be attached to surrounding structures, such as the muscle or skin. 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 approximately 5% of women presenting with breast cancer have advanced disease with distant metastases (where cancer cells have spread to other parts of the body), and that around 35% of those presenting with early or localised breast cancer will develop metastatic breast cancer in the 10 years following diagnosis.

HER2 is a receptor for a 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. HER2-positive breast cancer accounts for up to 25% of all metastatic breast cancers.

The role of current treatments 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. After disease has progressed on treatment with trastuzumab the NICE clinical guideline recommends that treatment with trastuzumab is stopped (unless disease progression is within the central nervous system alone). At this point patients may receive treatment with non-targeted chemotherapies such as capecitabine or vinorelbine. Lapatinib is a HER2 targeted treatment which in combination with capecitabine is also licensed for use at this point in the treatment pathway.

The technology

Trastuzumab emtansine (Kadcyla, Roche Products) is an antibody-drug conjugate. This combines anti-HER activity with targeted intracellular delivery. Trastuzumab emtansine is administered via intravenous infusion.

Trastuzumab emtansine does not currently have a UK marketing authorisation. It has received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) recommending the granting of a marketing authorisation for the treatment of adult patients with HER2-positive, unresectable locally advanced or metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for locally advanced or metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

Intervention	Trastuzumab emtansine
Population	People with HER2-positive, unresectable advanced or metastatic breast cancer whose disease has progressed after treatment with trastuzumab and a taxane.
Comparators	• lapatinib in combination with capecitabine • capecitabine • vinorelbine • trastuzumab in combination with capecitabine • trastuzumab in combination with vinorelbine

Outcomes	The outcome measures to be considered include: • progression free survival • overall survival • 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, 'Guidance on the use of trastuzumab for the treatment of advanced breast cancer'. Review suspended. Technology Appraisal No. 239, December 2011, 'Fulvestrant for the treatment of locally advanced or metastatic breast cancer'. Review proposal date August 2014. Technology Appraisal No. 250, April 2012, 'Eribulin for the treatment of locally advanced or metastatic breast cancer'. Review proposal date November 2014. Suspended technology appraisal, 'Lapatinib for breast cancer (for use in women with previously treated advanced or metastatic breast cancer)'. Technology Appraisal in preparation, 'Pertuzumab in combination with trastuzumab and docetaxel for treating HER2-positive metastatic or locally recurrent unresectable breast cancer'. Earliest anticipated date of publication: November 2013. Related Guidelines: Clinical guideline No. 81, February 2009 'Advanced breast cancer: diagnosis and treatment'. (replaces previous Technology Appraisals No. 30, 54 and 62). Review decision date 2013. Related NICE Pathways: NICE Pathway: Advanced breast cancer, Pathway created: May 2011, Last updated: September 2013 http://pathways.nice.org.uk/pathways/advanced-breast-cancer