NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Trastuzumab emtansine for the treatment of locally advanced or metastatic HER2-positive breast cancer after treatment with trastuzumab and a taxane

Draft scope (pre-referral)

Draft remit/appraisal objective

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

Background

Breast cancer is the most common cancer in the UK accounting for about 1 in 3 of all cancers in women. In 2009 there were 43,183 diagnoses of breast cancer in England and Wales. In 2010, there were around 11,600 deaths from breast cancer in the UK.

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 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. HER2-positive breast cancer accounts for up to 25% of all 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 (brand name unknown, Roche Products) combines the monoclonal antibody trastuzumab with the anti-microtubule agent maytansinoid DM1. 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 been studied in a clinical trial in comparison with lapatinib and capecitabine in people with locally advanced or metastatic HER2-positive breast cancer whose disease has progressed despite receiving prior treatment with trastuzumab and a taxane.

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

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. Suspended technology appraisal, 'Lapatinib for breast cancer (for use in women with previously treated advanced or metastatic breast cancer)'. 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.

Questions for consultation

Where is trastuzumab emtansine likely to be used in the pathway of care for people with locally advanced or metastatic HER2-positive breast cancer?

- Will trastuzumab emtansine be used after disease has progressed following treatment with trastuzumab used in the metastatic setting, or might it be used earlier in the treatment pathway in people who have had trastuzumab and a taxane as part of adjuvant treatment but whose

disease then recurs (i.e. disease previously untreated in the metastatic setting)?

Have the most appropriate comparators for trastuzumab emtansine for the treatment of locally advanced or metastatic HER2-positive 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?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which trastuzumab emtansine will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

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)