NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Lapatinib for the first-line treatment of metastatic hormone-sensitive breast cancer

Draft scope

Remit

To appraise the clinical and cost effectiveness of lapatinib within its licensed indication in combination with letrozole for the first-line treatment of metastatic hormone-sensitive breast cancer.

Background

Breast cancer is the most common cancer affecting women in the UK, accounting for nearly 1 in 3 of all cancers in women. In England and Wales, over 37,000 new cases were diagnosed in 2002, and there were over 11,000 deaths due to breast cancer in 2003. Many breast cancers are stimulated to grow and change by naturally occurring female sex hormones, oestrogen and progesterone. Tumours that have receptors to these hormones are more likely to respond to hormonal therapies (drugs or treatments that block the effects of hormones, or lower the levels of oestrogen and progesterone), and patients with such tumours tend to have a better prognosis. Approximately 15% to 20% of women with metastatic breast cancer have tumours which over-express HER2 (human epidermal growth factor). HER2 positive tumours are associated with a worse prognosis and reduced overall survival.

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 previous therapy, oestrogen receptor status, HER2 status and the extent of the disease. First-line therapy is usually an anthracycline-based regimen. Where an anthracycline is unsuitable (for example if the person has previously received anthracycline-based adjuvant therapy or has a contraindication to anthracyclines) NICE clinical guideline 81 recommends docetaxel monotherapy. Alternatively, combination therapy may be considered for people in whom a greater probability of response is important (NICE technology appraisal guidance No. 116 recommends gemcitabine in combination with paclitaxel). Vinorelbine or capecitabine should then be considered for subsequent lines of therapy for people with HER-2 negative breast cancer. For patients who are hormone receptor positive tamoxifen may be used, while for patients who are both post-menopausal and hormone receptor positive anastrozole or letrozole may be used. For patients with HER2 +ve tumours, trastuzumab in combination with either a taxane or an aromatase inhibitor may be used and vinorelbine or capecitabine may be considered if there is disease progression following treatment with trastuzumab.

The technology

Lapatinib (Tyverb, GlaxoSmithKline), is an oral therapy which inhibits the tyrosine kinase components of the ErbB2 (synonymous with HER2) receptor, and a second receptor, ErbB1, which have been implicated in the growth of various tumour types. Stimulation of ErbB1 and ErbB2 is associated with cell proliferation, and with multiple processes involved in tumour progression, invasion and metastasis. Lapatinib is being studied in clinical trials in combination with letrozole for the treatment of women with metastatic breast cancer who have not previously received treatment for metastatic disease.

Intervention(s)	Lapatinib in combination with letrozole
Population(s)	Post menopausal women with metastatic breast cancer which is oestrogen receptor and/or progesterone receptor positive and who have not previously received treatment for metastatic disease.
Standard comparators	First-line therapy for people with HER2- disease who have not previously been treated with anthracyclines: • anthracycline-based regimens When anthracyclines are not suitable (because the person has a contraindication to anthracyclines or has previously been treated with anthracyclines): • docetaxel as monotherapy • paclitaxel in combination with gemcitabine First-line therapy for people with HER2+ disease • Trastuzumab with or without anastrozole First line therapy for people who do not require chemotherapy • Aromatase inhibitors • Tamoxifen
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • time to progression • 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 If evidence allows the appraisal should consider a subgroup of patients based on HER2 positive status.
Related NICE recommendations	Related Technology Appraisals: NICE Appraisal Guidance No.34 – The use of trastuzumab for the treatment of advanced breast cancer, March 2002. Technology Appraisal No. 116, January 2007, 'Gemcitabine for the treatment of metastatic breast cancer.' Technology Appraisal No. 147 (terminated appraisal), June 2008, 'Bevacizumab for the first line treatment of metastatic breast cancer' Technology appraisal in preparation, 'Lapatinib for the treatment of women with previously treated advanced or metastatic breast cancer . Earliest anticipated date of publication: April 2009 Technology appraisal in preparation, 'Bevacizumab in combination with non-taxane chemotherapy for the first line treatment of metastatic breast cancer'. Earliest anticipated date of publication: TBC Related Guidelines: Clinical Guideline CG81, February 2009, Advanced breast cancer: diagnosis and treatment. Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (2004, CG014)

Questions for consultation

Have the most appropriate comparators for lapatinib been included in the scope? Are the comparators listed routinely used in clinical practice?

Are the subgroups suggested in 'other considerations appropriate? Are there any further 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?