NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of bevacizumab in combination with non-taxane chemotherapy within its licensed indication for the first-line treatment of metastatic breast cancer.

Background

Breast cancer is the most common malignancy affecting women in the UK. There were over 40,000 women and around 250 men newly diagnosed with breast cancer in England and Wales during 2007. Furthermore, there were around 12,000 deaths due to breast cancer in the UK in 2008; an average rate of 38.6 deaths per 100,000 women and 0.2 deaths per 100,000 men. 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 it is estimated that around 35% of those presenting with early or localised breast cancer will eventually develop metastatic breast cancer.

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, human epidermal growth factor receptor 2 (HER2) 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. Where an anthracycline is unsuitable (for example, if the person has previously received anthracycline-based adjuvant therapy or has a contraindication to anthracyclines) the clinical guideline recommends docetaxel monotherapy as a first-line treatment for advanced HER2-negative breast cancer. The guideline states that combination chemotherapy may be considered to treat patients with advanced breast cancer for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity. NICE technology appraisal guidance No. 116 recommends gemcitabine in combination with paclitaxel. Vinorelbine or capecitabine monotherapy should then be considered for subsequent lines of treatment.

The technology

Bevacizumab (Avastin, Roche Products) is a humanised anti-vascular endothelial growth factor (VEGF) monoclonal antibody that inhibits VEGF-induced signalling and inhibits VEGF-driven angiogenesis. This reduces vascularisation of tumours, thereby inhibiting tumour growth. Bevacizumab is administered by intravenous infusion.

Bevacizumab in combination with non-taxane chemotherapy (including anthracycline-based [doxorubicin or epirubicin] regimens or capecitabine) does not currently hold a UK marketing authorisation. Bevacizumab has been studied in clinical trials for the treatment of people with untreated metastatic breast cancer (HER2-negative) in combination with any one of three chemotherapy agents including anthracyclines, capecitabine and taxanes, compared with chemotherapy alone. The proposed marketing authorisation for bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer will be limited to people with HER2-negative metastatic breast cancer.

Bevacizumab in combination with paclitaxel or docetaxel has a marketing authorisation for first-line treatment of people with metastatic breast cancer. An appraisal of bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer is currently in progress.

Intervention	• Bevacizumab in combination with anthracyclines • Bevacizumab in combination with capecitabine
Population	Adults with untreated HER2-negative metastatic breast cancer for whom treatment with a taxane is unsuitable
Comparators	Bevacizumab in combination with anthracyclines should be compared with: • Anthracycline-based regimens without bevacizumab When anthracyclines are not suitable, comparators for bevacizumab in combination with capecitabine include: • Capecitabine monotherapy • Vinorelbine monotherapy
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	Potential subgroups such as by histology and hormone receptor status will be considered if evidence allows. Guidance will be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 147, June 2008 (Terminated), 'Bevacizumab for the first-line treatment of metastatic breast cancer'. Technology Appraisal in Preparation, 'Bevacizumab in combination with a taxane for the first-line treatment of HER2 negative metastatic breast cancer (to include a reinitiation of terminated TA147)'. Earliest anticipated date of publication November 2010. Technology Appraisal in Preparation, 'Fulvestrant for the treatment of locally advanced or metastatic breast cancer'. Earliest anticipated date of publication TBC. Related Guidelines: Clinical Guideline No. 81, February 2009, 'Advanced breast cancer: diagnosis and treatment'. This guidance replaces previous Technology Appraisals No. 30, 54 and 62. Review date February 2012.