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

Draft 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 300 men newly diagnosed with breast cancer in England and Wales during 2006. Furthermore, there were around 12,000 deaths due to breast cancer in the UK in 2007; an average rate of 38.6 deaths per 100,000 females and 0.3 deaths per 100 000 males. Between 16% and 20% of women (an estimated 6,000 to 8,000 women) presenting with breast cancer have advanced disease with distant metastases, and it is estimated that around 50% 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. Patients for whom chemotherapy is suitable may receive systemic sequential therapy using a number of chemotherapy agents including anthracyclines (doxorubicin, epirubicin and idarubicin), taxanes (docetaxel and paclitaxel), capecitabine, vinorelbine and gemcitabine.

First-line therapy is usually an anthracycline-based regimen, if an anthracycline is considered appropriate. 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 as a first-line treatment for advanced HER2-negative breast cancer. Alternatively, combination chemotherapy may be considered for people in whom a greater probability of response is important, and who are likely to tolerate additional toxicity. NICE technology appraisal guidance No. 116 recommends gemcitabine in combination with paclitaxel only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate. 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. There are also clinical studies that include patients with HER2-positive disease.

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(s)	Bevacizumab in combination with non-taxane chemotherapy (anthracyclines or capecitabine)
Population(s)	Adults with untreated metastatic breast cancer for whom treatment with a taxane is unsuitable
Comparators	• Anthracycline-based regimens without bevacizumab When anthracyclines are not suitable, comparators for bevacizumab in combination with capecitabine include: • Capecitabine 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 HER2 status and oestrogen 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. 34, March 2002, 'Guidance on the use of trastuzumab for the treatment of advanced breast cancer'. Currently being reviewed. Technology Appraisal No. 116, January 2007, 'Gemcitabine for the treatment of metastatic breast cancer'. Static guidance. 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. Technology Appraisal in Preparation, 'Lapatinib for the treatment of women with previously treated advanced or metastatic breast cancer'. Earliest anticipated date of publication TBC. 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 May

	2011. Technology Appraisal in Preparation, 'Trastuzumab as monotherapy and in combination with a taxane for the treatment of metastatic breast cancer (to include a review of TA34)'. Earliest anticipated date of publication October 2011. 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.

Questions for consultation

Is the population defined in the scope appropriate? Should HER2 status be specified in the population of the scope? If so, should the definition of the population by HER2 status vary depending on whether the combination with anthracycline-based regimens or capecitabine is being appraised?

Have the most appropriate comparators for the treatment of metastatic breast cancer for whom treatment with a taxane is unsuitable been included in the scope? Specifically, would vinorelbine be considered an appropriate comparator when anthracyclines are unsuitable?

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

What do you consider to be the relevant clinical outcomes and other potential health related benefits of bevacizumab in combination with non-taxane chemotherapy for the first-line treatment of metastatic breast cancer, particularly when compared with currently used treatment options?

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

Which process would be the most suitable for appraising this technology, the single technology or multiple technology process? (Information on these processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)