NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Bevacizumab in combination with standard chemotherapy for the second line treatment of HER2 negative metastatic breast cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of bevacizumab within its licensed indication in combination with chemotherapy for the second line treatment of human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer.

Background

Breast cancer is the most common malignancy affecting women in the UK. There were over 42,000 women and around 300 men newly diagnosed with breast cancer in England and Wales during 2008, and around 11,000 deaths 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, 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) patients should start treatment with docetaxel.

Second-line treatment options include taxane monotherapy (with either docetaxel or paclitaxel if not used as a first-line treatment), followed by vinorelbine or capecitabine monotherapy for subsequent lines of treatment. The guideline also states that combination chemotherapy (such as docetaxel in combination with capecitabine) 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 recommends gemcitabine in combination with paclitaxel as an option for the treatment of metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate (technology appraisal no. 116).

The technology

Bevacizumab (Avastin, Roche Products) is an antibody that specifically binds and blocks vascular endothelial growth factor (VEGF). VEGF is a key driver of tumour angiogenesis – an essential process of development and maintenance of blood vessels which is required for a tumour to grow and to spread to other parts of the body. Bevacizumab helps control tumour growth. It is administered by intravenous infusion.

Bevacizumab does not have a UK marketing authorisation for the second line treatment of HER2 negative metastatic breast cancer. It has been studied in clinical trials in combination with standard chemotherapy(taxanes, gemcitabine, capecitabine or vinorelbine) compared with chemotherapy alone in people with metastatic breast cancer that progressed during or following one chemotherapy regimen.

Bevacizumab has a UK marketing authorisation for the first line treatment of metastatic breast cancer in combination with paclitaxel. NICE does not recommend bevacizumab in combination with a taxane as a first line treatment for people with metastatic breast cancer (technology appraisal no. 214).

Intervention(s)	Bevacizumab in combination with standard chemotherapy
Population(s)	People with HER2-negative metastatic breast cancer previously treated with one chemotherapy regimen
Comparator(s)	• Docetaxel or paclitaxel (if not used as a first line treatment) • Docetaxel in combination with capecitabine • Vinorelbine • Capecitabine • Gemcitabine in combination with paclitaxel
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	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No 116, January 2007, 'Gemcitabine for the treatment of metastatic breast cancer'. Moved to static guidance list. Technology Appraisal No. 214, February 2011, 'Bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer' (replaces Technology Appraisal No. 147, 'Bevacizumab for the first-line treatment of metastatic breast cancer'). Review date July 2013. Technology Appraisal in Preparation 'Bevacizumab in combination with non-taxanes for first line metastatic breast cancer' (Suspended). Technology Appraisal in Preparation, 'Eribulin for the treatment of locally advanced or metastatic breast cancer'. Earliest anticipated date of publication December 2011. Proposed Technology Appraisal, 'Iniparib for the treatment of metastatic triple negative breast cancer', 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.

Questions for consultation

Have the most appropriate comparators for bevacizumab for the second-line treatment of HER2 negative metastatic 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?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

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)