NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Ixabepilone for locally advanced or metastatic breast cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ixabepilone within its licensed indication for the treatment of metastatic or locally advanced 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 38,000 new cases were diagnosed in 2003, and there were over 11,000 deaths due to breast cancer in 2004.

There are many risk factors that predispose women to developing breast cancer, the strongest being increasing age. Eighty percent of breast cancer occurs in post menopausal women (assuming average age of menopause is 50). Other risk factors include previous breast cancer, family history, early menarche, late menopause, number of children, genetic mutations and having children late or never having children.

Breast cancer is usually defined using a staging system developed by the American Joint committee on Cancer (AJCC) and the Tumour, Node and Metastasis Staging System (TNM). Advanced (or stage III) breast cancer denotes disease that is locally advanced and/or has spread to regional lymph nodes. Metastatic (or stage IV) breast cancer describes the presence of disease at distant sites such as the bone, liver, or lung (metastases). It has been estimated that more than 20% of women initially presenting with breast cancer have locally advanced disease or distant metastases. Approximately 40-50% of women presenting with early or localised breast cancer will eventually develop metastatic breast cancer. Symptoms include swelling, soreness, infection and inflammation of the breast and the nipple. In addition the potential for difficulties in breathing and chest pains if the cancer spreads to the lungs.

The role of current treatments for advanced and metastatic breast cancer is to prolong survival, maintain a good quality of life and palliate symptoms with minimal adverse events. The key decisions involving choice of treatment are based on previous treatment/therapy, oestrogen receptor status and the extent of the disease. Chemotherapy treatments are increasingly being targeted at subsets of patients with particular molecular characteristics.

The technology

Ixabepilone (Ixempra; Bristol-Myers Squibb Pharmaceuticals) is an epothilone B analogue which is reported to evade drug efflux, a mechanism which leads

to decline in concentrations of taxanes and other cytotoxic drugs in cancer cells.

Ixabepilone does not have a marketing authorisation in the UK. It is currently being investigated in clinical trials in women with non-resectable, locally advanced or metastatic breast cancer where previous cytotoxic chemotherapy has failed, either as monotherapy where previous chemotherapy has included anthracycline, taxanes and capecitabine or in combination with capecitabine where previous chemotherapy has included anthracycline and taxanes.

Intervention(s)	Ixabepilone monotherapy and in combination with capecitabine
Population(s)	People with locally advanced or metastatic breast cancer for whom previous cytotoxic chemotherapy has failed
Standard comparators	Capecitabine, vinorelbine and taxane containing regimens and other appropriate chemotherapy regimens in standard practice in England and Wales.
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate • health-related quality of life • adverse effects of treatment
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	If evidence allows, patient subgroups for whom the technology is particularly clinically or cost effective will be considered. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No.30, September 2001– The use of taxanes for the treatment of breast cancer. Technology Appraisal No.34, March 2002 – The use of trastuzumab for the treatment of advanced breast cancer. Technology Appraisal No.54, December 2002 – The use of vinorelbine for the treatment of advanced breast cancer. Technology Appraisal No.62, May 2003 – The use of capecitabine for the treatment of locally advanced or metastatic breast cancer. Technology Appraisal No. 116, January 2007 – Gemcitabine for the treatment of metastatic breast cancer. Technology Appraisal in preparation - Lapatinib for the treatment of previously treated women with advanced, metastatic or recurrent breast cancer. Earliest date of issue: TBC. Related guidelines: National Institute for Clinical Excellence (2002) Guidance on cancer services. Improving outcomes in breast cancer. *Manual update*. London: National Institute for Clinical Excellence. NICE Clinical Guideline No. 41 - Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care, October 2006. Related Guidelines in progress: NICE Clinical Guideline – Advanced breast cancer: diagnosis and treatment. Expected date of issue: February 2009. NICE Clinical Guideline – Early breast cancer: diagnosis and treatment. Expected date of issue: February 2009.