NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Fulvestrant for the treatment of locally advanced or metastatic breast cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of high dose (500mg) fulvestrant within its licensed indication for the treatment of locally advanced or metastatic breast cancer.

Background

Breast cancer is the most common malignancy affecting women in the UK accounting for 1 in 3 of all cancers in women. There were over 40,000 women and 300 men newly diagnosed with breast cancer in England and Wales during 2006. Furthermore, over 12,000 deaths due to breast cancer occurred in the UK in 2007, an average rate of 38.6 deaths per 100,000 women and 0.3 deaths per 100 000 men. Between 16% and 20% 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 50% of those presenting with early or localised breast cancer will eventually develop metastatic breast cancer.

The role of current treatments for advanced and metastatic breast cancer is to palliate symptoms, prolong survival and maintain a good quality of life with minimal adverse events. Endocrine (hormonal) therapy is appropriate for approximately 70% of people who have hormone receptor-positive advanced breast cancer. Endocrine treatment is not suitable for people with hormone receptor negative breast cancer. NICE clinical guideline 81 recommends that an aromatase inhibitor should be used for post-menopausal women with oestrogen receptor positive breast cancer, either as a first-line treatment or if they have previously been treated with adjuvant endocrine therapy (such as tamoxifen). Tamoxifen is the recommended first-line therapy for men with hormone receptor positive advanced breast cancer. In clinical practice, individuals may be treated with several endocrine therapies, such as aromatase inhibitors, oestrogen receptor antagonists and progestogens, either as monotherapy or as combinations. Appropriate endocrine treatment options are determined by prior endocrine treatment, the extent and duration of any previous response to treatment, and menopausal status.

The technology

Fulvestrant (Faslodex, AstraZeneca) is an oestrogen antagonist belonging to a class of agents known as selective oestrogen receptor down-regulators

(SERDs). Fulvestrant is administered by intramuscular injection every four weeks.

High-dose (500mg) fulvestrant is not currently licensed for use in the UK. It has been studied in clinical trials as a monotherapy and as an adjuvant treatment to aromatase inhibitors for postmenopausal women with advanced or metastatic breast cancer. High-dose fulvestrant has been compared with low-dose fulvestrant, exemestane and anastrozole.

Fulvestrant (250mg) has marketing authorisation for the treatment of oestrogen receptor positive metastatic or locally advanced breast cancer in postmenopausal women in whom disease progresses or relapses while on, or after, other anti-oestrogen therapy.

Intervention(s)	Fulvestrant (500mg)
Population(s)	Postmenopausal women with oestrogen receptor positive metastatic or locally advanced breast cancer, whose disease progresses or has relapsed while on or after endocrine (anti-oestrogen) therapy.
Comparators	Monotherapy or combination regimens of the following anti-oestrogen (endocrine) treatments: • Low-dose (250mg) fulvestrant • oestrogen-receptor antagonists (tamoxifen, toremifene) • aromatase inhibitors (anastrozole, exemestane, letrozole) • Progestogens (megestrol acetate, medroxyprogesterone acetate)
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, Jan 2007, 'Gemcitabine for the treatment of metastatic breast cancer'. Technology Appraisal No.112, Nov 2006, 'Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer'. Technology Appraisal No. 34, Mar 2002, 'Guidance on the use of trastuzumab for the treatment of advanced 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 Jul 2010. 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 Aug 2010. Technology Appraisal in Preparation, 'Lapatinib for breast cancer (for use in women with previously treated advanced or metastatic breast cancer)'. Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, 'Sunitinib in combination with capecitabine for the treatment of advanced and/or metastatic breast cancer'. Earliest anticipated date of publication Oct 2011. Technology Appraisal in Preparation, 'Sunitinib in

	combination with a taxane for the first-line treatment of advanced and/or metastatic breast cancer'. Earliest anticipated date of publication TBC. Related Clinical Guidelines Clinical Guideline No. 81, Feb 2009, 'Advanced breast cancer: diagnosis and treatment'. This guidance replaces previous Technology Appraisals Nos. 30, 54 and 62. Clinical Guideline No. 80, Feb 2009, 'Breast cancer (early & locally advanced): diagnosis and treatment'.

Questions for consultation

Have the most appropriate comparators for the treatment of advanced and/or metastatic breast cancer been included in the scope? Are the comparators listed routinely used in clinical practice?

Are endocrine therapies such as androgens, diethylstilboestrol and trilostane routinely used in clinical practice for the treatment of advanced and/or metastatic breast cancer, and if so, should they also be included as comparators?

Are there any 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, such as patients who have had prior endocrine treatment?

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?

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 these processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)