Kate Moore
Technology Appraisal Project Manager
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13 September 2011

Dear Ms Moore,

Fulvestrant for the treatment of locally advanced or metastatic breast cancer

Breakthrough Breast Cancer is a pioneering charity committed to the prevention, treatment and ultimate eradication of breast cancer. We fight on three fronts: research, campaigning and education. Our aim is to bring together the best minds and rally the support of all those whose lives have been, or may one day be, affected by the disease. The result will save lives and change futures – by removing the fear of breast cancer for good.

This submission reflects the views of Breakthrough, based on our experience of working with people with personal experience of, or who are concerned about, breast cancer. We regularly consult with members of our Campaigns and Advocacy Network (Breakthrough CAN) for their views on a range of breast cancer issues. Originally founded by women with personal experience of breast cancer, Breakthrough CAN brings together over 1,700 individuals, regional groups and national organisations to campaign for improvements in breast cancer research, treatments and services. Through supporting and training members to become patient advocates in their own right, Breakthrough CAN aims to increase the influence of patients in decisions regarding breast cancer issues.

Breakthrough welcomes the opportunity to comment on the appraisal consultation document regarding the use of fulvestrant for the treatment of locally advanced or metastatic breast cancer in people whose disease has progressed during or after treatment with tamoxifen.

Has all of the relevant evidence been taken into account?

Approximately two thirds of women with breast cancer are diagnosed with ER+ breast cancer and could potentially benefit from fulvestrant, an oestrogen receptor antagonist and selective oestrogen receptor down regulator. A significant proportion of breast cancer patients will develop advanced and metastatic disease and treatment options for these women are limited. This drug gives an additional treatment option for women living with advanced or metastatic disease. As metastatic breast cancer is not curable, it is essential that treatment options which could delay progression or improve survival are made available for this patient group. Patients typically have limited treatment options in the metastatic setting and therefore the need for safe and effective new medicines in this patient group is relatively urgent.

As the committee states, fulvestrant was found to extend life by at least 3 additional months compared to the currently used aromatase inhibitors anastrazole and letrozole and increased time to progression compared to anastrazole. Delaying time to progression and knowing there are active hormonal treatment options available is very important to the women we speak with. Delayed time to disease progression can improve the quality of life of these women. With fulvestrant patients can expect symptom control, which brings with it improved quality of life, including social functioning (e.g. continuing to work, maintaining relationships and the ability to participate in activities such as going on holiday) and spending more quality time with family and friends.

Fulvestrant at 500mg is well-tolerated[1]. The appraisal committee heard from a patient taking fulvestrant that the disadvantages of monthly injections and the side effects of fulvestrant were outweighed by the benefits of remaining fit and well. In addition, the monthly administration of the drug enables patients to have regular communication with their specialist team.

The importance of delayed progression and improved survival for women with advanced and metastatic breast cancer must not be underestimated. Although we recognise that fulvestrant does not meet all of the criteria for special consideration as an end of life treatment, we believe that the benefits it would bring to patients should be fully considered.

When women are no longer benefiting from active hormonal treatments often the only option left for them is chemotherapy. Many women are keen to delay chemotherapy in favour of other treatments for as long as possible, as the side effects and disruption to their lives associated with chemotherapy can have a significant impact on their quality of life. The committee concluded that patients value having another treatment option after aromatase inhibitors and anti-oestrogen therapies because of its value as a treatment and also because it can delay chemotherapy.

NICE guidance recommends aromatase inhibitors as adjuvant treatment for most postmenopausal women with oestrogen receptor positive early breast cancer. If a woman who has received aromatase inhibitors goes on to develop advanced or metastatic disease she will not usually be offered aromatase inhibitors again, further reducing her already limited treatment options.

Although this appraisal considers the use of fulvestrant following tamoxifen but not aromatase inhibitor treatment, it is important to note that fulvestrant is most commonly used after aromatase inhibitors. The appraisal committee considered that the most likely position of fulvestrant in UK clinical practice would remain as a third-line or fourth-line treatment after therapy with aromatase inhibitors and/or an anti-oestrogen therapy, which was outside the remit of this appraisal. It is worth noting that the clinical specialist the committee consulted stated that there is little or no clinical evidence about the optimal treatment sequence for advanced breast cancer beyond first-line treatment. We would welcome appraisal of use in this setting as it could provide women with a much needed treatment option.

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[1] Di Leo A, Jerusalem G, Petruzelka L *et al.*(2009) CONFIRM: Phase III, randomized, parallel-group trial comparing fulvestrant 250mg vs fulvestrant 500mg in postmenopausal women with oestrogen receptor-positive advanced breast cancer. *Cancer Res,* 69 (24 Suppl): Abstract nr 25.

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

We are disappointed that the Appraisal Committee is unable to recommend fulvestrant for the treatment of locally advanced or metastatic breast cancer. We acknowledge that the cost per QALY gained is relatively high in this setting. However, we understand that the manufacturer is attempting to set up an access scheme which could potentially reduce the cost per QALY to a more acceptable level.

Fulvestrant is more commonly used as a 3rd or 4th line treatment when aromatase inhibitors are no longer effective, than in the place of aromatase inhibitors as reviewed here. Use following aromatase inhibitor failure is often in place of chemotherapy. Although fulvestrant has a high cost per QALY compared to aromatase inhibitors it would be useful to compare the cost of fulvestrant to the cost of chemotherapy.

As mentioned previously, there are currently very few options for women with advanced and metastatic breast cancer and fulvestrant could have a large positive impact on their quality of life. The importance of this should not be underestimated.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

It is disappointing that the committee is unable to recommend fulvestrant as an alternative to aromatase inhibitors for the treatment of oestrogen-receptor-positive, locally advanced or metastatic breast cancer in postmenopausal women whose cancer has relapsed on or after adjuvant anti-oestrogen therapy, or who have disease progression on anti-oestrogen therapy. There are very limited treatment options for these women and as a patient organisation, Breakthrough Breast Cancer would like to emphasise the importance of further treatments for this group.

We accept that the cost per QALY gained is relatively high compared to aromatase inhibitors. We hope that an access scheme may bring this down making fulvestrant more cost effective.

We would welcome appraisal of fulvestrant in the setting in which it is most often used – following disease progression on aromatase inhibitors. If this drug is not made available for use by the NHS the implication is that active treatment by hormone therapy will cease following completion of aromatase inhibitor therapy.

Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

None of which we are aware.