csas
Commissioning Support
Appraisals Service

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5th September 2011

National Institute for Health and Clinical Excellence

Dear Ms Moore

RE: Appraisal Consultation Document, Fulvestrant (Metastatic Breast Cancer)

On behalf of Commissioning Support, Appraisals Service (CSAS), Solutions for Public Health, we would like to submit our comments on the appraisal consultation document for 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.

We are in agreement with the recommendations in the ACD not to recommend fulvestrant for this indication as on the basis of the evidence considered it is unlikely that this treatment can be considered clinically and cost effective in real life clinical practice.

- **This technology is not a cost effective use of NHS resources.** The committee concluded that the ICER for fulvestrant in its licensed dose was likely to be at least £35,000 per QALY gained compared with the aromatase inhibitor anastrozole. However, considerable uncertainty remained regarding this estimate.
- **Unit costs of fulvestrant are significantly higher than current standard** treatment. The cost of fulvestrant is currently £1,044.82 for the first month, and £522.41 in subsequent months (excluding VAT). This is based on BNF 61 prices for a 250mg prefilled syringe. The manufacturer reports that this pack size will no longer be available after 2012 due to the licensed dose now being 500mg monthly. This may affect costs. This compares to a cost for anastrozole 1mg daily of £74.48 per month.
- **The relative clinical effectiveness of fulvestrant compared to aromatase inhibitors is uncertain.** There are no RCTs directly comparing the licensed dose of fulvestrant (500mg) against aromatase inhibitors (AIs). A network meta-analysis conducted by the manufacturer to allow these comparisons to be made indirectly suggested no significant differences in overall survival between fulvestrant and the AIs anastrozole and letrozole. Fulvestrant 500mg may offer a longer time to progression (TTP) compared to anastrozole however, there was heterogeneity between the studies included and limitations to the statistical methods used which meant that there was a high degree of uncertainty about the reliability of these results.
- **Evidence submitted by the manufacturer does not reflect current UK clinical practice.** In the UK, fulvestrant is considered as a third or fourth line treatment after aromatase inhibitor treatment. This use is outside the current marketing authorisation and therefore outside the remit of this technology appraisal. It is therefore unclear where fulvestrant would fit in the care pathway.

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- **The exact number of patients who would be eligible for fulvestrant in its licensed indication is uncertain, but is likely to be small.** The manufacturer estimates that 2,200 women would be eligible under the existing license. Clinical advice offered to NICE suggested that most postmenopausal women now receive an aromatase inhibitor as adjuvant hormone therapy for early breast cancer or as first-line treatment if presenting with advanced breast cancer. This limits the use of fulvestrant under its current license.
- **There were limitations to the quality of the evidence:** There were no RCTs comparing the licensed dose of fulvestrant against aromatase inhibitors. A network meta-analysis was conducted by the manufacturer to allow these comparisons to be made indirectly, but there were limitations to the methods used, including possible bias from the selection of the trials, heterogeneity between the trials included, and problems with the statistical methods used. These limitations reduce the reliability of the results of these analyses.
- **Fulvestrant does not offer any improvement in overall survival, nor does it meet the criteria for end of life considerations.** There is no evidence indicating an increase in survival.

If you require any further information please contact me directly: Phone: [redacted] email [redacted].

Yours sincerely

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