Letter Appraisal Committee to GE Feb 2010

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Vice-chair, Technology Appraisal Committee
NICE

Mr Andrew Dillon
for Guidance Executive
NICE

16 February 2010

Dear Andrew

I refer to the Guidance Executive document 'Lapatinib for women with previously treated advanced or metastatic breast cancer' dated January 2010 sent over your name.

The Appraisal Committee reviewed this document and its more detailed content at its meeting on 16 February 2010, as I undertook to do on behalf of Jane Adam, Committee Chair. The GE request for reconsideration relates to a particular aspect of choice of comparators in this matter, and the Committee reviewed the evidence on that and consequential aspects. We are grateful to Gillian Leng (Deputy Chief Executive) for her attendance in your necessary absence.

The Appraisal Committee is as you know composed of people with backgrounds in a wide variety of roles in the NHS. These include commissioners of care and primary and secondary health care physicians, as well as health economists, clinical trialists, people from patient associations, and public heath physicians. Nevertheless, while a wide variety of points were made by diverse members in discussing the matter, there was complete uniformity of opinion that the Committee's original opinion, with clarification, should stand.

Though comforted by the comments of the Appeal Panel in 2009, the Committee did not take these into account in reaching its views on this occasion. I also asked that the Committee approach the arguments afresh, on the evidence as presented on this occasion and previously, and without a need to feel they were being asked to defend their previous views – the discussion was appropriate to that standard. The Committee was cognisant of:

- its previous detailed deliberations in this area (see pre-appeal FAD and draft FAD January 2010)
- the NICE clinical guideline views on continuation of trastuzumab post progression both with and without brain metastases
- its more recent consideration of the sub-group of women with brain metastases in the context of the discussions about the NICE supplementary guidance on appraising treatments used at the end of life.

The Committee noted that it appeared to be the view of the Guidance Executive that use of trastuzumab post-progression on that drug was both occurring, as the Committee had previously accepted, and that replacement of that use by lapatinib and capecitabine (in combination) in the context of the previously accepted GSK patient access scheme could possibly release resources within the NHS without detriment to the health of those women with advanced breast cancer.

The Committee noted that it had well documented previously the large uncertainties surrounding the relative effectiveness of lapatinib in this situation. It noted that the GBG26 study, the source of effectiveness data on trastuzumab post-progression, had a number of weaknesses in data presentation. It was further noted that the assumptions

surrounding vial wastage and 3-weekly use of trastuzumab by the manufacturer of lapatinib might well be biased in a way that favoured the resource costs of lapatinib over trastuzumab, and that these had been shown in sensitivity analyses to have marked effects on the ICERs. The Committee noted that GSK had suggested that trastuzumab was being continued in women who appeared to still be gaining some benefit from trastuzumab, having minimal progression of some type, which would increase the effectiveness and relative effectiveness in this selected population. However the Committee also acknowledged that this population might be less responsive to trastuzumab, being trastuzumab failures, something presently unknown. In these circumstances, even on a narrow view, the Committee could not recommend the use of lapatinib in progressors on trastuzumab.

The Committee noted that it would be difficult to ensure the implementation of any recommendation that lapatinib should replace trastuzumab in a defined population of women progressing on the drug. The Committee believed that any such recommendation could significantly expand the population in some Cancer Networks who received either drug following progression of disease on trastuzumab, and that this would be detrimental to the efficient deployment of NHS resources, given that currently such women would receive non-biological therapy if any.

The Committee noted its previous discussions on women with brain metastases, and the view of the NICE guidelines GDG on this topic that women with CNS metastases on trastuzumab should have it continued. The Committee noted that this must mean that the GDG believed that there was the possibility of continuing efficacy of trastuzumab in this situation outside the brain. The Committee noted the uncertainty as to whether, in this group of women in whom metastasis had occurred but in whom there was no evidence of such outside the brain, the efficacy of trastuzumab was different from those in whom progression has occurred outside the central nervous system. It had felt that in these circumstances it was inappropriate to suggest replacing trastuzumab with a drug of limited evidence both in the individual and in clinical trials, known to the Committee to be due to report after 2012. The Committee could not then change its view concerning this sub-group.

The Committee felt that, in addition to more narrowly based arguments that it should not endorse lapatinib in this circumstance (above), methods guidance that it should follow best practice should take precedence over guidance it should follow routine care. The Committee noted in this respect the NICE guideline that trastuzumab should not be used post-progression except in the context of metastases solely within the CNS. Accordingly the Committee was persuaded that it should not change its previous recommendations.

The Committee also considered the wider impact on the NHS of a decision to recommend lapatinib (even as an option) in women progressing on a drug used out of licensed indication and against NICE guidelines. While Committee members said they would not happy with the broader effects of such a decision, these issues were not taken into account in reaching the views expressed above.

I would be happy to clarify any points on the Committee's behalf.

Philip

Professor Philip Home, Vice-chair and Chair of lapatinib appraisal.