Friday 5th October 2006

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BY E-MAIL

Dear Carole,

SINGLE TECHNOLOGY APPRAISAL –
Gemcitabine for treatment of metastatic breast cancer

Thank you for sending us the Appraisal Consultation Document (ACD) and supportive documentation for the above technology appraisal. As a commentator within this appraisal, Roche would like to provide feedback on one particular issue only.

Indirect Comparisons

A key issue arising from this negative ACD for gemcitabine appears to us to relate to the synthesis of the available clinical effectiveness data. According to the ERG Report, the manufacturer did not adequately account for the observed heterogeneity across the numerous clinical trials utilised within the economic analysis (ACD, section 4.6).

Roche would like to provide feedback on the broader issue relating to the apparent requirement and expectation of both ERGs and of NICE for the manufacturer to perform more elaborate methods of indirect comparison of clinical effectiveness evidence.

It is often the case that the comparators selected in clinical trials may not be optimal for the purposes of UK HTA. There are at least three reasons for this:

1) Clinical practice in the UK may, for historical reasons, be different from that in a majority of countries where clinical trials or registration studies are conducted

2) Clinical practice may have progressed to the extent that what seemed an appropriate comparator at the time of clinical study commencement might now be considered sub-optimal

3) Clinical practice in the UK may currently differ due to resource or other constraints which result in standard treatments different from those more generally acknowledged as optimal and therefore used as clinical trial comparators.

Under such circumstances it may be that an intervention being reviewed by NICE has to be appraised using indirect comparisons. Although all would agree that this is less than ideal, it is incumbent upon NICE to try and make such a comparison. As section 5.2.3.3 of the Guide to Methods states:

"*There are always likely to be deficiencies in the evidence base available for HTA assessment…despite such weaknesses in the evidence base, decisions still have to be made about the use of technologies*".

The existing "Guide to the Methods of Technology Appraisal" (April 2004) does provide some guidance on evidence synthesis and on managing heterogeneity (section 5.4). However, no explicit reference or guidance is provided on the use of specific methods such as those apparently adopted by SHTAC during the course of this appraisal (which are not published in the ERG Report).

Consequently Roche wonders whether it would be useful for NICE to update the "Guide to Methods of Technology Appraisal" to provide greater detail on when methods of indirect comparison should be adopted in the preparation of HTA submissions and indeed on what methods might be preferable. This could help in the future, allay situations where manufacturers might be criticised for not adopting particular methodologies which are not outlined explicitly within the "Guide to Methods of Technology Appraisal".

I hope that these comments are helpful.

Yours sincerely,