[redacted]

Thursday 28th October 2010

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BY E-MAIL

Re: Multiple Technology Appraisal – NICE appraisal of lapatinib and trastuzumab for metastatic breast cancer – Liverpool Assessment Report

[redacted]

Please find below our initial comments to the Liverpool Assessment Report. If you require any further clarification or information then please do not hesitate to contact us.

Yours sincerely,

[redacted]

Page	Comment
7 ; 19	The Assessment Group incorrectly described the licensed indications for lapatinib. It should be noted that lapatinib in combination with capecitabine is not licensed for 1st line mBC but rather "*following prior therapy, which must have included anthracyclines and taxanes and therapy with trastuzumab in the metastatic setting*".
8; 26	The Assessment Group incorrectly described the chemotherapies licensed for use in combination with trastuzumab in the metastatic setting. These should include only taxanes (paclitaxel or docetaxel). The Assessment Group described fluorouracil (5FU), methotrexate, cyclophosphamide and epirubicin combination treatment which suggests the trastuzumab metastatic and early breast cancer licenses have been confused.
15	The Assessment Group states that 'Most patients who present for HER+/HR+ mBC are likely to have been previously treated for early breast cancer and very probably with regimens including trastuzumab'. Roche market research suggests that approximately 70% of all new HER2+ metastatic breast cancer patients are trastuzumab-naïve.
20	The Assessment Group notes that trastuzumab is administered weekly in the metastatic setting. This is incorrect and inconsistent with their acceptance later in the report that 3-weekly administration of trastuzumab is the common schedule among metastatic breast cancer patients in the UK.
38	In Table 4, the OS medians for the HR+/HER2+ population appear to be switched.
44	We can confirm that in Table 8 the latest updated PFS figures (HR=0.55 (95% CI 0.41 – 0.74)) are based on the ITT population rather than only those with centrally confirmed HR status.
72	The AG clinical advisors state that cardiac monitoring occurs every 3 months. This is in contrast with a Roche panel of clinical advisors who agree this occurs less frequently – usually every 4 months. This is aligned with the recent NCRI guidelines published last year which advises, in mBC, patients should have ECHO/MUGA at 4 and 8 months and if cardiac function is stable further assessment should be completed at doctor/patient's discretion (Jones *et al*, British Journal of Cancer (2009) 100, 684 – 692.)
77	The Assessment Group note that in the first committee meeting for trastuzumab in mGC the Appraisal Committee 'considered the size of the eligible patient population and was not satisfied that the population for which TRA is licensed met the criterion of a small patient population'. It should be noted that following the second committee meeting for trastuzumab in HER2+ mGC this opinion was reversed with the committee concluding that it was appropriate to consider trastuzumab under NICE's supplementary end of life guidance. This appraisal is currently subject to a positive FAD restricting the use of trastuzumab to patients with IHC3+ HER2+ mGC.
86-91; 94; 97-98	Insufficient detail due to the removal of confidential information limits our ability to review the AG's economic analysis. However, at least one inconsistency has been noted in the findings. Table 29 reports that the life years gained due to the addition of trastuzumab is less than 0.5 years which is also described on page 97 stating that trastuzumab provides 'a modest expected mean health gain per patient (less than 6 months life extension …)'. This figure seems counter to the approximate 8 month survival advantage estimated on page 90 and appears to significantly under-estimate the survival advantage granted by trastuzumab with consideration of the confounding influence of cross-over and the observed imbalance in 2nd line chemotherapy use.