National Institute for Health and Clinical Excellence

Centre for Health Technology Evaluation

Pro-forma Response

ERG report

Erlotinib for the first-line treatment of EGFR-TK mutation positive non-small-cell lung cancer

Please find enclosed the ERG report prepared for this appraisal.

You are asked to check the ERG report from Liverpool Reviews and Implementation Group (LRiG) to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by **5pm, Wednesday 21 December 2011** using the below proforma comments table. All factual errors will be highlighted in a report and presented to the Appraisal Committee and will subsequently be published on the NICE website with the Evaluation report.

The attached proforma document should act as a method of detailing any inaccuracies found and how and why they should be corrected.

Issue 1 The use of the term 'MTC'

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
Page 14. The statement '**the manufacturer has conducted a systematic review and mixed treatment comparison (MTC)**' should be amended. An MTC is a specific form of network meta-analysis in which both direct and indirect evidence of the relative efficacy of treatments is pooled. In our submission a simple indirect comparison of erlotinib and gefitinib was conducted utilising direct evidence on the efficacy of erlotinib compared to doublet chemotherapy and direct evidence on the efficacy gefitinib compared to doublet chemotherapy. No indirect links were utilised. The use of the term 'MTC' is therefore incorrect. This term is also used on page 17 and repeatedly throughout later pages.	The statement on page 14 should be amended to '**the manufacturer has conducted a systematic review and indirect treatment comparison (ITC)**' All other references to the 'MTC' in respect to related Roche analysis should be amended to 'ITC'.	The use of the term MTC is factually incorrect and may mislead the Committee and any Consultees or Commentators who do not review the Manufacturer's submission in full.	ERG to amend submitted report and replace *mixed treatment comparison/MTC* with *indirect comparison/IC* where appropriate

Issue 2 Comments on the scoping workshop for this appraisal

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
Page 15. The statement 'Thus the consultees at the scoping workshop	This sentence should be removed.	This sentence is factually inaccurate and so should be	The ERG to remove sentence

considered that for people with NSCLC of adenocarcinoma or large cell carcinoma histology, pemetrexed is an appropriate comparator to erlotinib' is factually incorrect and is not reflective of what was discussed at the scoping workshop. At the scoping workshop for this appraisal consultees agreed that pemetrexed/cisplatin would only be an appropriate comparator to erlotinib in patients unsuitable for gefitinib (but not in EGFR M+ patients who were suitable for gefitinib who would receive gefitinib). Whilst the final scope issued then deviated from this conclusion (without explanation) and included pemetrexed/cisplatin as a comparator in all EGFR M+ patients it is factually incorrect to state that this was the conclusion reached in the scoping meeting.		removed.	

Issue 3 Use of the term "artificially low ICER"

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
Page 8. The following statement in bold is not factually accurate when commenting on the manufacturer's model: "*Yields OS gains for the first-line treatment of EGFR M+ patients with erlotinib and gefitinib that are not demonstrated by the published RCT*	Either remove this statement or provide significant qualification and a better balance in reflecting the uncertainty in validating predicted survival outcomes using clinical trials confounded by incomplete follow-up and patient crossover.	This represents the opening summary of the ERG critique of the Roche Economic model. Reporting this subjective judgement on uncertain scientific evidence as a statement of fact unfairly compromises the credibility and	ERG to remove statement 'leading to artificially low ICER estimates'

*evidence (**leading to artificially low ICER estimates**)".* This is reported as a statement of fact when in reality until longer term survival data is able to validate the predicted outcomes, no one can say with certainty whether the Roche survival estimates are an under or over-estimation. Longer term survival analysis and extrapolation is routinely utilised by NICE to estimate longer term outcomes. The ERG statement suggests absence of evidence is evidence of absence. In the context of estimating overall survival within oncology studies powered to evaluate progression free-survival and containing patient cross-over; this is not necessarily the case.	One suggestion is to reflect the alternative possibility the ICER could be "*artificially high*" given we are speculating on future as yet unknown long term survival benefits for the patients in question.	confidence in the manufacturer ICER and economic model.	