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Dr Carole Longson
Appraisal Programme Director
National Institute for Health and Clinical Excellence
MidCity Place
71 High Holborn
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Dear Dr Longson

RE: Eli Lilly and Company response to Technical Assessment report (TAR) – Pemetrexed/cisplatin in Malignant Pleural Mesothelioma (MPM)

Thank you for forwarding the Technical Assessment Report on pemetrexed for the treatment of mesothelioma, compiled by the Liverpool Review and Implementation Group (LRiG).

In general we believe the TAR is a clear overview of the use of pemetrexed/cisplatin in the treatment of MPM. There are however three key points we would like to raise and three errata. These are discussed below.

1. Individual Patient Data (IPD) – Availability for analysis

Lilly is disappointed in LRiG's interpretation of Lilly's assistance during the assessment particular since LRiG will be aware of the numerous emails between Lilly and LRiG/NICE, specifically in respect of access to IPD.

To the greatest extent possible, Lilly provided LRiG with such information it was legally entitled to provide, as Lilly was (and always will be) bound by the terms of relevant consent documents. In its letter of 1 August 2005, Lilly informed LRiG that the consent form completed by patients on inclusion to the trial precluded Lilly from providing full datasets of IPD as shared with the FDA. The consent forms used by Lilly contain the following statement related to patient consent:

> "*Data obtained from this study that does not identify you individually will be given to the sponsor and/or its representatives and may be published or given to regulatory authorities in [name of country study being conducted in] or other countries in which regulatory approval of ALIMTA may be sought. Your original medical records may be reviewed by the sponsor and/or its representatives, the Ethical Review Board for this study, and regulatory authorities for the purpose of verifying clinical trial procedures and/or data*."

The FDA independently confirmed to LRiG that access to the IPD could only be made on formal application by a UK government department.

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Requesting IPD from manufacturers/sponsors is therefore unacceptable, not only for commercial reasons, but also for regulatory, confidentiality and patient-consent reasons. Patient consent in clinical trials is given specifically for regulatory purposes, and permission is not given for sharing data with non-regulatory bodies.

Therefore we would be grateful for the Appraisal Committee's understanding of the difficulties facing companies in having to satisfy requests for IPD.

In summary, we believe we co-operated fully with LRiG because we provided them with the full working model which provides exactly the same data we used for our submission. We believe this is more than is commonly provided by companies for the purpose of NICE review.

2. Model 2

Whilst we are aware that LRiG have acknowledged that there are data gaps with currently used UK comparators in mesothelioma, we are disappointed that they have considered the attempt to model current practice as 'fruitless'.

This model was completed at the specific request of NICE and LRiG as stated in the NICE final scope and the meeting with LRiG on 15 June 2005. At this meeting we explained to LRiG the issues with the (lack of) evidence in trying to compare pemetrexed/cisplatin against the UK comparators, but their representatives were adamant that every attempt should be made to model current UK practice.

Model 2 took significant time and effort on our part and whilst we recognise there are deficiencies in the evidence base, we believe this is the first systematic attempt to review the evidence (clinical and market research data) on MVP, vinorelbine and best supportive care (BSC) in mesothelioma, pending the results of the MSO1 study.

We are aware that the Appraisal Committee will have access to our executive summary which provides a summary of model 2 results but we believe that the TAR should include at least a brief review of model 2 thus ensuring that the Appraisal Committee is not denied insight into the systematic review of the evidence base for the treatment of MPM.

3. Reporting of cost/LYG estimates

Whilst we understand that NICE prefer cost/QALY analyses, the final scope for this appraisal requested cost/LYG analyses because it is recognised that this is an end-stage disease and prolonging survival is considered the most important aim of treatment. In addition there are no utility estimates for mesothelioma therefore cost/LYG estimates should be included in the summary section of the TAR.

Errata

- **5.2 Economic Impact of pemetrexed plus cisplatin for MPM**

The TAR states that 'pemetrexed is over 40 times the price of cisplatin.'

We are concerned that this is an inaccurate since the price of pemetrexed is approximately £1600/cycle and cisplatin is £84/cycle. This statement, if included, should therefore be corrected to reflect the latter.

- **5.3.1 Identification of studies**

This section reports on one comparative economic abstract found through a systematic search. However on 7 November 2005 we forwarded copies of a poster presented at the European Cancer

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Conference in October 2005 to LRiG which was based on the economic case submitted to the SMC earlier that year [1]. The appraisal by the SMC resulted in a positive recommendation [2]. Therefore the abstract by Davey et al [3] was not the only publicly information available and this should be so stated.

In the interests of including all relevant data we suggest inclusion of this poster and the positive recommendation by the SMC.

- **7.4.1 Base case cost-effectiveness results**

Despite reference to company estimates, table 7D refers only to the estimates obtained by the assessment group. This sentence should be amended to include reference to table 6C which contain our estimates or table 7D should be enlarged to include the company estimates.

We would be grateful if the TAR could be amended in light of our comments above. Should you have any questions please do not hesitate to contact me.

Kind regards.

Yours sincerely

Dr Debbie Stephenson, MBBS MRCPsych FFPM
Medical Advisor and Head of HTA Strategy

References

1. Chetty M et al. Economic impact of adopting pemetrexed plus cisplatin for malignant pleural mesothelioma into Scottish clinical practice. Presented at the European Cancer Conference, Paris. October 2005.

2. SMC Pemetrexed 500mg infusion (Alimta®) (192/05)- **Eli Lilly** 05 August 2005: http://www.scottishmedicines.org.uk/updocs/pemetrexed%20500mg%20infusion%20(Alimta)%20(192-05).pdf

3. Davey P et al. Value for money of pemetrexed plus cisplatin versus cisplatin alone in the treatment of MPM (conference presentation). International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conference 2004.