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10th January 2014

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Dear Helen

Pemetrexed for continuation maintenance treatment of non-squamous non-small-cell lung cancer [ID489]: Lilly response to NICE's revised estimates of eligible patient numbers for consideration of pemetrexed under the 'End of Life' supplementary criteria

Thank you for the opportunity to review and respond to the updated estimates of the eligible patient population for pemetrexed in advance of the fourth Appraisal Committee meeting.

We have reviewed the updated estimates based on the latest 2012 NLCA data and accept the patient numbers for first-line NSCLC (N=4,898) provided in your letter. We have also updated the numbers for continuation maintenance in accordance with the latest 2012 NLCA data for consistency. This increases the patient population from N=632 to N=654, since the audit data show that 57.2% of PS 0-1 non-squamous NSCLC patients received chemotherapy. As stated in our response to the third ACD (submitted 18th December), we believe the estimated number of patients with performance status (PS) 2 eligible for second-line treatment with pemetrexed should be N=194.

We sought updated estimates for pemetrexed in malignant pleural mesothelioma (MPM), to ensure consistency with the updated NSCLC estimates. The latest data from the NLCA 2012 (personal communication, [redacted] on behalf of NLCA project team, 9th January 2014) show that 61.1% of mesothelioma patients with advanced disease are eligible for chemotherapy. As a result, the total population of patients with advanced mesothelioma and PS 0-1 eligible to receive pemetrexed in combination with cisplatin is N=1,056 (see enclosed Table 1 for calculations).

To summarise, the total number of patients eligible for pemetrexed treatment for all indications is as follows:

- PS 0-1 non-squamous NSCLC patients eligible for pemetrexed first-line: N=4,898
- Patients eligible for continuation maintenance treatment with pemetrexed: N=654
- PS 2 patients eligible for pemetrexed second-line treatment: N=194
- PS 0-1 advanced malignant pleural mesothelioma (MPM) patients eligible for pemetrexed: N=1,056

We believe that the updated maximum plausible estimate for the eligible patient population for pemetrexed across all licensed indications is **6,803 patients** (i.e., 4,898 PS 0-1 first-line NSCLC + 654 continuation maintenance + 194 PS 2 patients second-line + 1,056 PS 0-1 advanced disease mesothelioma patients).

Of note, the estimated 4,898 patients eligible for first-line treatment includes 10%-15% (N=490 to N=735) of patients who are EGFR mutation positive (Final scope, Afatinib EGFR positive locally advanced or metastatic NSCLC. ID556; Costing statement for TA258). In current clinical practice and in accordance with NICE guidance, EGFR positive patients would be eligible for erlotinib or gefitinib rather than pemetrexed.

The maximum plausible estimate, revised by the NICE technical team and Lilly using the latest NLCA data, demonstrates that the eligible patient population is **6,803** and pemetrexed continuation maintenance should therefore be considered under the 'End of Life' supplementary criteria.

Yours sincerely

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cc: Meindert Boysen

Encl: Table 1. Calculation of the size of the pemetrexed-eligible population based on patients first seen in 2011 and 2012

References:

1. National Lung Cancer Audit Report 2013. http://www.hscic.gov.uk/catalogue/PUB12719/clin-audi-supp-prog-lung-nlca-2013-rep.pdf

2. NICE. Final scope. Afatinib for EGFR positive locally advanced or metastatic NSCLC. ID 556. May 2013.

3. NICE. Erlotinib for first-line treatment of locally advanced or metastatic EGFR mutation positive NSCLC. Costing statement. London: NICE; June 2012.

4. Personal communication, Dr. Beckett on behalf of the National Lung Cancer Audit project team, 9th January 2014.

Table 1. Calculation of the size of the pemetrexed-eligible population based on patients first seen in 2011 and 2012 (Lilly modifications in italics)

	NLCA report 2013 Audit period 2012
Number of PS 0-1 NSCLC Stage IIIB or IV	7,203
Non-squamous histology	68%
Potential population eligible for first-line therapy with pemetrexed	**4,898**[1]
Receive first-line chemotherapy	*57.2%*[2]
Receive pemetrexed plus cisplatin	40.00%
Eligible for pemetrexed continuation maintenance treatment	58.40%
Potential population eligible within maintenance licence	**654**
Population eligible for pemetrexed in a second-line setting[3]	***194***
Number of patients with mesothelioma	1,964
Patients with advanced disease	88.00%
Patients with PS 0-1[4]	*61.10%*
Potential population eligible for pemetrexed - mesothelioma	**1,056**
Estimated total population eligible for pemetrexed	**6,803**

[1] The estimated 4,898 patients eligible for first-line treatment includes 10%-15% (N = 490 to N=735) of patients who are EGFR mutation positive In current clinical practice and in accordance with NICE guidance, EGFR positive patients would be eligible for erlotinib or gefitinib rather than pemetrexed.

[2]Updated as per the NLCA 2012 data

[3]As per Lilly response to third ACD submitted 18th December.

[4]Updated based on personal communication from Dr. Beckett on behalf of NLCA project team, 9th January 2014, as described in the above response.