A review of the economic evaluation of oral gefitinib (Iressa®) for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with activating mutations of EGFR

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Summary

1. In June 2010, AstraZeneca submitted an economic dossier on the cost-effectiveness and potential budget impact of oral gefitinib tablets (Iressa®) for the first and second line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating mutations of the epidermal growth factor receptor (EGFR).

2. Gefitinib was compared to carboplatin plus paclitaxel doublet chemotherapy (carboplatin-paclitaxel) for the first line treatment of EGFR mutation positive (m+) patients with locally advanced or metastatic NSCLC. A Markov model was developed to perform a cost utility analysis over a five year time horizon. The efficacy data for the model was obtained from a sub-group analysis of EGFR m+ patients (n=261) from the IPASS study. Gefitinib was directly compared with carboplatin-paclitaxel as first line therapy in this study. Gefitinib significantly prolonged progression free survival in NSCLC EGFR m+ patients compared with doublet chemotherapy. However, there was no statistically significant difference in overall survival between the two arms. Furthermore, patients with EGFR negative mutations were shown to have poorer outcomes on gefitinib compared with doublet chemotherapy.

3. Gefitinib was compared to erlotinib (Tarceva®) for the second line treatment of EGFR m+ patients with locally advanced or metastatic NSCLC. Efficacy of gefitinib as a second line therapy in EGFR m+ patients was demonstrated in the INTEREST trial; a multicentre, randomised, open-label, phase III trial of gefitinib versus docetaxel in patients who were treated with previous platinum chemotherapy and had locally advanced or metastatic NSCLC. A cost minimisation analysis was conducted, based on the assumption that there was no meaningful difference in QALYs between gefitinib and erlotinib. The Review Team had concerns regarding the strength of the evidence to support the assumption of equal safety and efficacy of gefitinib and erlotinib. The evidence was based on an unpublished randomised study of small sample size and a retrospective observational study.

4. In the pooled data set from the ISEL (Iressa Survival Evaluation in Lung Cancer, Lancet 2005), INTEREST and IPASS phase III clinical trials, the most frequently

reported adverse effects of gefitinib are diarrhoea, skin rash and raised liver aminotransferase levels. Interstitial lung disease occurred in 1.3 % of patients.

5. The base-case incremental cost-effectiveness ratio (ICER) for the first line treatment of EGFR m+ patients with gefitinib as compared with carboplatin-paclitaxel was **€110,564/QALY.** The ICER ranged from approximately €85,000 to €137,000/QALY when the price to the wholesaler was varied +/-20%.

6. The net cumulative discounted cost to the HSE of reimbursing gefitinib as second line treatment for EGFR m+ patients was estimated to result in **savings of approximately €28,000** assuming a treatment duration of 6.5 months and patent expiry of gefitinib in the second half of 2014. If a patent extension is granted for gefitinib, and there is no price reduction in 2014, introduction of gefitinib as second line therapy would be **cost-neutral** to the HSE.

7. In the first line treatment setting it was estimated that the incremental five year budget impact was approximately €0.88 million per year. In the second line treatment setting, the incremental 5 year budget impact for the treatment of EGFR m+ patients was estimated to result in cost savings of €32,736.

8. Gefitinib is the first oral therapy for first line treatment of advanced or metastatic NSCLC. It offers advantages for patients because it is an oral medication which can be taken at home. The mechanism of action of gefitinib allows targeting of therapy at EGFR m+ patients. This is an innovative approach to treatment and results in improved progression free survival compared with standard doublet chemotherapy. Gefitinib is associated with fewer adverse effects compared with platinum-based chemotherapy. However, **gefitinib cannot be recommended as a cost-effective option for the first line treatment of EGFR m+ patients** with locally advanced or metastatic NSCLC as the **ICER of €110,564/QALY** is substantially higher than the usual willingness to pay threshold.

9. Finally, the NCPE Review Team had concerns about the assumption that there was no meaningful difference in QALYs between gefitinib and erlotinib. It was estimated that **replacement of erlotinib with gefitinib in the second line treatment of EGFR m+ patients could be cost neutral or cost saving to the HSE**, depending on the patent status of gefitinib in 2014.