Addendum 2

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

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

This report was commissioned by the NIHR HTA Programme as project number 11/08

Completed 13th March 2012

CONTAINS CIC

UNIVERSITY OF LIVERPOOL

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP

A MEMBER OF THE RUSSELL GROUP

1 INTRODUCTION

The Appraisal Consultation Document (ACD) issued by NICE requires the manufacturer of erlotinib to make two changes to the submitted economic model:

- to ensure that the estimated progression-free survival (PFS) values for patients receiving erlotinib and gefitinib are equal

- to ensure that the assumed utility value in PFS for patients receiving erlotinib and gefitinib are equal

This amended model should then be used to carry out a sensitivity analysis relating to the proportion of patients in PFS at day 60 (who would trigger payment under the gefitinib patient access scheme [PAS]).

2 MODIFICATIONS TO ECONOMIC MODEL

The manufacturer has provided a modified version of their model, in order to implement these requests. The equality of PFS estimates was achieved by simply fixing the hazard ratio of gefitinib vs. erlotinib to a value of 1.0. Since this parameter directly governs the overall survival (OS) estimate for gefitinib, it ensures that there is no OS difference between gefitinib and erlotinib.

The amendments required to ensure that the PFS utility values take a common value in both arms of the evaluation are more complex. The manufacturer has chosen to maintain the logic of the Nafees' [1] utility model, which depends on the proportion of patients showing objective response together with the proportions suffering from two key grade 3/4 adverse events (AEs) (rash and diarrhoea). By setting the response rate ratio of gefitinib vs erlotinib to 1.0, equivalence is achieved for this component of utility. For the two adverse events, the manufacturer assumes that erlotinib incidence rates also apply to gefitinib. This approach is successful in equalising PFS utility estimates, but creates a further anomaly because the AEs occur less frequently when patients are treated with gefitinib than with erlotinib, and this therefore masks a difference in the costs associated with AEs. An alternative approach is to override the Nafees[1] logic directly, using a single common utility value for both options, and maintain the differential AE rates with their associated costs. The effect of the overall cost calculations of preserving the differential AE costs is small, amounting to an additional £5.24 per patient when treatment is with erlotinib.

In order to facilitate sensitivity analysis of the proportion of gefitinib patients who would be charged under the PAS (requiring additional gefitinib treatment at day 60), a single new parameter has been created by the manufacturer which overrides the proportion of erlotinib patients in the EURTAC[2] trial who were still on treatment at 60 days. The base case value for this parameter is 0.8, which may be compared to the proportion in PFS at the same time (0.877). A minor related modification is made to

the calculation of the proportion of patients on treatment at 30 days, to ensure consistency (i.e. that the number of patients on treatment at 30 days cannot exceed those on treatment at 60 days).

3 COST OF ADMINISTERING THE GEFITINIB PATIENT ACCESS SCHEME

Consideration was not given to the cost of administering the gefitinib PAS at the time of the appraisal of gefitinib. The manufacturer of erlotinib has included a method for estimating this cost in their model, involving five separate elements (patient registration, ordering a single pack, invoicing per patient, accountancy relating to each pack ordered, and 'query management'). The first, third and fifth of these are considered one-off costs for each patient and amount to £70, while the other two elements are applied every time a new pack in required (£35 each 30 days). This is in addition to the normal dispensing costs. In total, this approach generates a discounted mean cost of £438 per patient.

The ERG is concerned that this approach may significantly overstate the administration costs of the PAS. Individual ordering and the processing of each pack issued are unlikely to occur in practice. It is more likely that once prescribed, a patient will be treated out of bulk orders related to the duration of treatment of the average patient (13.5 months), with annual retrospective reconciliation. There is unlikely to be an issue of expiry of bulk stocks, as gefitinib has a shelf life of 4 years.

If regular pack ordering is dismissed as already included in the cost of dispensing, then the cost of administering the PAS reduces to just £70 per patient. If it is assumed that ordering/reconciliation is required only annually then the discounted PAS administration cost of gefitinib is estimated at between £111 and £118 per patient.

4 COST-MINIMISATION: ERG REVISED MODEL RESULTS

The modifications made in the model to PFS and the utility values for PFS have the effect of ensuring that there are no differences between erlotinib and gefitinib in terms of OS, PFS or quality-adjusted life-years (QALYs). Therefore the economic analysis reduces to a simple cost-minimisation analysis, considering the net balance of cost per patient over a range of possible proportions of gefitinib patients incurring PAS treatment costs from 80% to 100%.

The following table shows results based on using the ERG's alternative method of equalising utilities, and a reduced gefitinib PAS administration cost (£111 - £122 per patient). This suggests that erlotinib and gefitinib incur equivalent net costs if approximately 95% of gefitinib patients remain on treatment at day 60. The erlotinib option is the cheaper option for proportions greater than 95%, and is more expensive for proportions less than 95%.

Additional analyses requested in ACD - updated estimates with ERG amendments

Proportion of patients receiving erlotinib or gefitinib on day 60	Gefitinib Drug Costs	Gefitinib PAS Costs	Erlotinib Drug Cost	Incremental Cost (E vs G)	Incremental QALYs (E vs G)
1.00 (maximum)	£12,200	£118	[redacted]	[redacted]	[redacted]
0.99	£12,078	£118	[redacted]	[redacted]	[redacted]
0.98	£11,956	£117	[redacted]	[redacted]	[redacted]
0.97	£11,834	£117	[redacted]	[redacted]	[redacted]
0.96	£11,712	£117	[redacted]	[redacted]	[redacted]
0.95	£11,590	£116	[redacted]	[redacted]	[redacted]
0.94	£11,468	£116	[redacted]	[redacted]	[redacted]
0.93	£11,346	£116	[redacted]	[redacted]	[redacted]
0.92	£11,224	£115	[redacted]	[redacted]	[redacted]
0.91	£11,102	£115	[redacted]	[redacted]	[redacted]
0.9	£10,980	£115	[redacted]	[redacted]	[redacted]
0.89	£10,858	£114	[redacted]	[redacted]	[redacted]
0.88	£10,736	£114	[redacted]	[redacted]	[redacted]
0.87	£10,614	£113	[redacted]	[redacted]	[redacted]
0.86	£10,492	£113	[redacted]	[redacted]	[redacted]
0.85	£10,370	£113	[redacted]	[redacted]	[redacted]
0.84	£10,248	£112	[redacted]	[redacted]	[redacted]
0.83	£10,126	£112	[redacted]	[redacted]	[redacted]
0.82	£10,004	£112	[redacted]	[redacted]	[redacted]
0.81	£9,882	£111	[redacted]	[redacted]	[redacted]
0.80 (base case)	£9,760	£111	[redacted]	[redacted]	[redacted]

5 REFERENCES

1. Nafees B, Stafford M, Gavriel S, Bhalla S, Watkins J. Health state utilities for non small cell lung cancer. Health and Quality of Life Outcomes. 2008;6(84).
2. Roche. EURTAC - Clinical study report (ML20650) 2011.