NICE National Institute for Health and Care Excellence

NICE guidance

Erlotinib monotherapy for maintenance treatment of non-small-cell lung cancer

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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1 Recommendations

1.1 Erlotinib monotherapy is not recommended for maintenance treatment in people with locally advanced or metastatic non-small-cell lung cancer who have stable disease after platinum-based first-line chemotherapy.

1.2 People currently receiving erlotinib monotherapy for maintenance treatment of locally advanced or metastatic non-small-cell lung cancer who have stable disease after platinum-based first-line chemotherapy should have the option to continue treatment until they and their clinician consider it appropriate to stop.

2 Information about erlotinib

2.1 Erlotinib (Tarceva, Roche Products) is an orally active inhibitor of the epidermal growth factor receptor (EGFR) tyrosine kinase. It has a UK marketing authorisation 'as monotherapy for maintenance treatment in patients with locally advanced or metastatic non-small cell lung cancer with stable disease after 4 cycles of standard platinum-based first-line chemotherapy'. For further information see the summary of product characteristics.

2.2 Undesirable effects of erlotinib treatment include diarrhoea, rash, anorexia, gastrointestinal bleeding, liver function test abnormalities and keratitis. For full details of side effects and contraindications, see the summary of product characteristics.

2.3 Erlotinib is given orally at a recommended dose of 150 mg/day. The normal acquisition cost of a pack of 30 tablets (150 mg) is £1,631.53 (excluding VAT; BNF, edition 60). The manufacturer of erlotinib has agreed a patient access scheme with the Department of Health in which the acquisition cost of erlotinib is reduced by 14.5% and deducted at the time of supply to the NHS (that is, £1,394.96 for a pack of 30 tablets [150 mg]). The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS. Costs may vary in different settings because of negotiated procurement discounts.

3 Committee discussion

The manufacturer's submission

The Appraisal Committee considered evidence submitted by the manufacturer of erlotinib and a review of this submission by the Evidence Review Group (ERG).

3.1 The manufacturer approached the decision problem by providing clinical and cost-effectiveness evidence for erlotinib maintenance monotherapy compared with best supportive care in patients with stage 3B or stage 4 squamous or non-squamous non-small-cell lung cancer who had stable disease after treatment with standard platinum-based first-line chemotherapy. Best supportive care included palliative radiotherapy, corticosteroids, analgesia and other symptomatic treatments and watchful waiting alone. In the economic evaluation the manufacturer provided combined and separate analyses for patients with squamous and non-squamous disease. The group of patients with non-squamous disease was further divided into 2 analyses: firstly those who were not eligible for pemetrexed maintenance therapy (that is, patients who received pemetrexed in combination with cisplatin as first-line treatment), with best supportive care as the comparator; and secondly those who were eligible for pemetrexed maintenance therapy (that is, patients who have received first-line treatment with platinum-based chemotherapy which did not include pemetrexed), with pemetrexed as the comparator. The manufacturer noted a lack of head-to-head clinical evidence comparing erlotinib with pemetrexed.

3.2 At the time of the manufacturer's original evidence submission, the marketing authorisation for erlotinib had not been granted and the population who would be covered by the marketing authorisation was unclear. Subsequently, erlotinib received a marketing authorisation for the maintenance treatment of a subgroup of patients with locally advanced or metastatic non-small-cell lung cancer, that is, patients with stable disease after standard platinum-based first-line chemotherapy. Because of this, some of the evidence included in the manufacturer's original submission was not relevant and further evidence for the population covered by the marketing authorisation was required. The manufacturer provided additional clinical and cost-effectiveness evidence for

patients with stable disease after first-line chemotherapy in response to consultation on the first appraisal consultation document.

3.3 The key evidence submitted by the manufacturer for the clinical effectiveness of erlotinib came from a randomised double-blind controlled trial comparing erlotinib with placebo in patients with advanced or metastatic non-small-cell lung cancer whose disease had not progressed following platinum-based first-line chemotherapy (the SATURN trial). This population included patients whose disease was either stable after first-line chemotherapy, or had responded to first-line chemotherapy. Stable disease was defined according to the Response Evaluation Criteria in Solid Tumours (RECIST) as tumour shrinkage that is not sufficient to be classed as a partial response and tumour increase that is not sufficient to be classed as progressive disease.

3.4 Patients were included in the SATURN trial if their disease had not progressed after 4 cycles of a standard, platinum-based chemotherapy doublet (2 chemotherapy drugs, 1 of which is platinum based), if they had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1 and their life expectancy was at least 12 weeks. The primary outcome of the trial was progression-free survival, defined as the time between randomisation and the date of the first documented disease progression, or death from any cause. Secondary outcomes included overall survival (defined as the time between randomisation and death), time to disease progression, response rates (assessed by the RECIST criteria) and quality of life (assessed by the Functional Assessment of Cancer Therapy – Lung [FACT-L] questionnaire). RECIST criteria were assessed by computed tomography (CT) scans every 6 weeks.

3.5 The SATURN trial included 889 patients, of whom 487 (55%) had stable disease after first-line chemotherapy. Of the patients with stable disease, approximately 30% had an ECOG performance status of 0 and 70% had an ECOG performance status of 1 at study entry, 20% had never smoked and 61% had non-squamous disease. Fifty percent of patients were tested for EGFR mutation status and of these 11% had activated EGFR mutations. The most common first-line treatments for patients in the whole trial population were gemcitabine plus carboplatin (28%), gemcitabine plus cisplatin (26%), and paclitaxel plus carboplatin (19%). None of the patients with non-squamous disease received combination chemotherapy with cisplatin and pemetrexed, now the most commonly prescribed first-line

regimen in UK clinical practice for this histological subtype of non-small-cell lung cancer. Most patients (48%) were from Eastern Europe, 21% were from south-east Asia and 1% were from the UK. The mean age of patients was 60 years. The proportion of patients who had at least 1 post-study treatment was 72% in the placebo group and 71% in the erlotinib group, with 21% of patients in the placebo group and 11% in the erlotinib group receiving subsequent treatment with a tyrosine kinase inhibitor (such as erlotinib or gefitinib). The proportion of patients with stable disease who had further systemic therapy after the study was 63% in the placebo group and 61% in the erlotinib group, with 21% of patients in the placebo group and 9% in the erlotinib group receiving subsequent treatment with either erlotinib or gefitinib. Of the 50% of patients with stable disease who were tested, the incidence of activated EGFR mutation was 6% in both the placebo and the erlotinib groups. The manufacturer stated that there were no imbalances between treatment arms when clinical, molecular, or geographical parameters were considered or when prior radiotherapy, subsequent systemic treatments and time to start of investigational treatment were analysed.

3.6 The manufacturer did not provide separate demographic analyses for the squamous and non-squamous disease groups in response to consultation on the first appraisal consultation document. However, during consultation on the second appraisal consultation document, the manufacturer indicated that although the baseline characteristics of known prognostic significance in the stable, squamous disease group were reasonably balanced between the erlotinib and best supportive care arms, this was not the case for the non-squamous disease group. Data from the SATURN trial showed that for the population with stable non-squamous disease, 30% of patients in the erlotinib group and 38% in the placebo group had an ECOG status of 0, and 25% of patients in the erlotinib group and 31% in the placebo group had never smoked. The manufacturer stated that because of these imbalances, the true overall survival benefit from erlotinib in the non-squamous disease group is likely to be confounded in favour of the best supportive care group.

3.7 For patients with stable disease after first-line chemotherapy, median progression-free survival was 12.1 weeks in the erlotinib group compared with 11.3 weeks in the placebo group (hazard ratio [HR] 0.68; 95% confidence interval [CI] 0.56 to 0.83, $p<0.0001$). Median overall survival was 11.9 months in the erlotinib group compared with 9.6 months in the placebo group, a difference of

2.3 months (HR 0.72; 95% CI 0.59 to 0.89, p=0.0019). The increase in progression-free survival associated with erlotinib was similar in patients with squamous disease (HR 0.69; 95% CI 0.51 to 0.93, n=190) and non-squamous disease (HR 0.69; 95% CI 0.54 to 0.87, n=297). The gain in median overall survival associated with erlotinib for patients with squamous disease was 3.0 months (HR 0.67; 95% CI 0.48 to 0.92) and 3.1 months for patients with non-squamous disease (HR 0.76; 95% CI 0.59 to 1.00). There were no statistically significant differences between the erlotinib and placebo groups in quality-of-life measures. In response to consultation on the first appraisal consultation document, the manufacturer provided estimates for the mean overall survival benefit associated with erlotinib for patients with squamous and non-squamous disease (4.5 months and 4.2 months respectively). The mean overall survival estimate for the whole stable disease population was 3.3 months.

3.8 Subgroup analyses were carried out by the manufacturer in patients with stable disease after first-line chemotherapy by EGFR immunohistochemistry (IHC) status, stage of disease, first-line chemotherapy regimen received, ECOG performance status, smoking status, geographical region, age, race and gender. Erlotinib was associated with a greater median overall survival benefit for patients with EGFR IHC-positive tumours (HR 0.65; 95% CI 0.51 to 0.88, p value not reported), for patients who had never smoked (HR 0.56; 95% CI 0.32 to 0.97, p value not reported), and for women (HR 0.55; 95% CI 0.35 to 0.87, p value not reported) compared with the whole stable disease population. In covariate analyses from the manufacturer of the whole stable SATURN population, south-east Asian patients had a greater progression-free survival benefit from erlotinib than white patients (covariate effect HR 0.78; p=0.0214), as did patients who had never smoked compared with current smokers (covariate effect HR 1.46; p=0.0003). In addition, the small subgroup of patients with activated EGFR mutations were also shown to gain substantially more benefit from erlotinib than the trial population as a whole (HR for progression-free survival 0.23; 95% CI 0.12 to 0.45).

3.9 During consultation on the second appraisal consultation document, the manufacturer provided adjusted analyses comparing erlotinib with best supportive care in patients with stable, non-squamous disease from the SATURN trial. The analysis suggested that when the data were adjusted for good ECOG performance status and smoking status (never smoked), patients with these

characteristics had an improved rate of overall survival after treatment with erlotinib compared with the whole stable, non-squamous disease population (HR 0.71; 95% CI 0.54 to 0.93). The estimate of overall survival was even higher (HR 0.63; 95% CI 0.41 to 0.96) when the analysis was repeated only in patients without an EGFR mutation (that is, the patients who are likely to receive erlotinib in UK clinical practice due to the growing use of gefitinib in patients with an EGFR mutation). In light of these analyses, the manufacturer stated that the overall survival benefit from erlotinib in the non-squamous disease population may have been underestimated in the SATURN trial.

3.10 In response to the second appraisal consultation document, the manufacturer provided patient characteristics for the squamous disease group to allay the Committee's concerns that the population in the SATURN trial may not be representative of patients seen in the UK. In particular, they showed that only 0.5% of patients with squamous disease had an EGFR mutation, 6.9% had never smoked and 7.9% were Asian. Given the relatively low incidence of patients with these prognostic factors, the manufacturer stated that they would not have a large impact on the overall survival benefit observed in the SATURN trial for the squamous disease group relative to what would be achieved in UK clinical practice.

3.11 The most common adverse events associated with erlotinib for the whole SATURN population were rash (49% in the erlotinib group and 6% in the placebo group) and diarrhoea (20% in the erlotinib group and 5% in the placebo group). In the stable disease subgroup, more patients in the erlotinib group had an adverse event of any kind than in the placebo group (78% compared with 58%). There were 23 deaths in the erlotinib group and 22 in the placebo group during the active treatment phase.

3.12 In the original submission, the manufacturer carried out an indirect analysis of erlotinib and pemetrexed in patients with non-squamous disease using data from a randomised controlled trial of pemetrexed maintenance treatment versus placebo in patients with locally advanced or metastatic non-small-cell lung cancer (the JMEN trial). This analysis included patients with stable disease but also included patients whose disease had responded to first-line treatment with platinum-based chemotherapy. The latter group are not covered by the marketing authorisation for erlotinib. In the additional evidence submission, received during

consultation on the first appraisal consultation document, the manufacturer stated that an indirect comparison of the SATURN and JMEN trials was not possible because no data on the efficacy of pemetrexed in patients with stable, non-squamous disease from the JMEN trial were publicly available. The manufacturer also stated that an indirect analysis was not considered appropriate because of differences in the populations in the 2 trials.

3.13 In the original submission, the manufacturer submitted economic analyses for 3 different patient populations, 2 of which included patients who were not covered by the marketing authorisation, that is, patients whose disease had responded to treatment. The only economic analysis that reflected the population covered by the marketing authorisation was the comparison of erlotinib with best supportive care in patients with stable disease. In response to consultation on the first appraisal consultation document, the manufacturer submitted 4 new economic analyses that included the population covered by the marketing authorisation:

- erlotinib compared with best supportive care in all patients with stable disease
- erlotinib compared with best supportive care in patients with stable, squamous disease
- erlotinib compared with best supportive care in patients with stable, non-squamous disease who were not eligible for pemetrexed maintenance treatment
- erlotinib compared with pemetrexed in patients with stable, non-squamous disease who were eligible for pemetrexed maintenance treatment.

3.14 The manufacturer's new economic analyses used a model with a cycle length of 1 month and a 15-year time horizon. The model included 3 health states: progression-free survival, progressed (defined as the time from first treatment relapse until death), and death. All patients were assumed to start in the progression-free survival health state (after first-line chemotherapy). At the end of each cycle, they could remain in this state, move to the progressed health state or die.

3.15 For the comparison of erlotinib with best supportive care, the risks of disease progression were taken from the SATURN trial. For the comparison of erlotinib

with pemetrexed, the base case assumed equal efficacy of pemetrexed and erlotinib. Additional relative efficacy scenarios were modelled, ranging from assuming greater efficacy of pemetrexed (in progression-free survival and overall survival) to assuming greater efficacy of erlotinib.

3.16 In the new economic analyses, the manufacturer used the same utility values as those used in NICE's technology appraisal guidance on pemetrexed for the maintenance treatment of non-small-cell lung cancer. The utility values for the progression-free survival health state were 0.6732 for the erlotinib group and 0.6628 for the placebo group. The utility value for the progressed health state was 0.53.

3.17 The new economic analyses included costs for treatment (erlotinib and pemetrexed), best supportive care, adverse events, and post-progression treatment. Costs for erlotinib were based on the patient access scheme (see section 2.3) and the treatment duration from the SATURN trial. Drug wastage was estimated based on when treatment stopped in the SATURN trial. The average per-patient drug costs for erlotinib were £7,148 for the overall stable disease population, £6,644 for patients with stable, squamous disease, and £7,976 for patients with stable, non-squamous disease. Pemetrexed costs were based on the list price to the NHS (BNF 58) and doses were based on the distribution of body surface area of patients with stable, non-squamous disease in the SATURN trial. The average per-patient drug cost for pemetrexed was £13,062. Costs for best supportive care were based on the average cost of specialist palliative care per cancer death per year reported in a publication by NICE and the University of Sheffield (2004). This is the same methodology used in other NICE technology appraisal guidance on treatments for non-small-cell lung cancer (pemetrexed for the first-line treatment of non-small-cell lung cancer and pemetrexed for the maintenance treatment of non-small-cell lung cancer). The best supportive care costs also included costs of regular monitoring (3-monthly hospital visits consisting of a consultant appointment and an outpatient CT scan).

3.18 The costs of adverse events associated with erlotinib were based on those used in NICE's previous technology appraisal guidance on erlotinib for the treatment of non-small-cell lung cancer (now replaced by NICE's technology appraisal guidance on erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy), and adjusted for inflation. The costs of

adverse events associated with pemetrexed were the same as those used in NICE's technology appraisal guidance on pemetrexed for the first-line treatment of non-small-cell lung cancer. Post-progression treatment costs were based on various sources including the BNF 58 and other NICE technology appraisal guidance (pemetrexed for the first-line treatment of non-small-cell lung cancer, and pemetrexed for the maintenance treatment of non-small-cell lung cancer). Data on the number and type of post-progression treatments were collected in the SATURN trial. Because there was a lack of data on post-progression treatment from the JMEN trial, the manufacturer assumed that the costs associated with pemetrexed would be the same as those for the placebo group of the SATURN trial.

3.19 In the manufacturer's original submission, the incremental cost-effectiveness ratio (ICER) for the comparison of erlotinib with best supportive care in patients with stable disease was £47,743 per quality-adjusted life year (QALY) gained (incremental cost £7,747 and incremental benefit 0.162 QALYs). In response to the first appraisal consultation document the manufacturer revised assumptions about how much time a patient spent on treatment in the progression-free health state and the costs attributed to post-progression best supportive care, resulting in an ICER of £39,936 per QALY gained (incremental cost £7,813, incremental benefit 0.196 QALYs) for all patients with stable disease. In response to the second appraisal consultation document the manufacturer provided a revised ICER of £40,792 per QALY gained (incremental cost £7,737, incremental benefit 0.190 QALYs) for the stable disease population, using survival estimates proposed by the ERG. For patients with stable, squamous disease the ICER for erlotinib was £35,491 per QALY gained compared with best supportive care (incremental cost £7,339, incremental benefit 0.207 QALYs). In patients with stable, non-squamous disease the ICER for erlotinib was £40,020 per QALY gained compared with best supportive care (incremental cost £8,696, incremental benefit 0.218 QALYs). For the comparison of erlotinib with pemetrexed in patients with stable, non-squamous disease, the cost of erlotinib was £7,531 lower than the cost of pemetrexed. Therefore, when erlotinib was assumed to have equal or better efficacy than pemetrexed, erlotinib dominated pemetrexed (that is, it had lower costs and better efficacy). In the manufacturer's various relative efficacy scenarios, the ICER for erlotinib compared with pemetrexed ranged from £77,598 saved per QALY lost (when erlotinib was assumed to have 10% better progression-free survival and 10% worse overall survival than pemetrexed) to

£511,351 saved per QALY lost (when erlotinib was assumed to have 10% worse progression-free survival and the same overall survival as pemetrexed).

3.20 The manufacturer conducted a number of deterministic sensitivity analyses. The factors that had the greatest impact on the ICERs for erlotinib compared with best supportive care were assuming that a patient spent all their time on treatment in the progression-free health state (£44,942 per QALY gained for the stable population) and using the best supportive care costs from NICE's previous technology appraisal guidance on erlotinib for the treatment of non-small-cell lung cancer (now replaced by NICE's technology appraisal guidance on erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy) rather than those from NICE's technology appraisal guidance on pemetrexed for the first-line treatment of non-small-cell lung cancer, and pemetrexed for the maintenance treatment of non-small-cell lung cancer (£44,745 per QALY gained for the stable population). The maximum ICERs for patients with stable, squamous disease and for those with stable, non-squamous disease were £40,599 per QALY gained (compared with £35,491 in the base case) and £44,589 per QALY gained (compared with £40,020 in the base case) respectively.

3.21 The ERG reviewed the clinical evidence originally submitted by the manufacturer and the additional evidence provided during consultation. It noted that the extent to which patients and investigators were truly blind to treatment allocation throughout the SATURN trial was uncertain because patients in the erlotinib group were significantly more likely to develop a rash and suffer from diarrhoea than patients in the placebo group. The ERG queried whether the results of the SATURN trial could be generalised to the UK because the trial included very few UK patients and the population was younger and fitter than would be seen in UK clinical practice. It also commented that a greater proportion of patients had first-line treatment with paclitaxel in the trial than would occur in UK clinical practice and no patients had first-line treatment that included pemetrexed, which is now the most common first-line treatment for patients with non-squamous disease (following publication of NICE's technology appraisal guidance on pemetrexed for the first-line treatment of non-small-cell lung cancer). The ERG noted inconsistencies in the reporting of post-study treatments between the manufacturer's submission and the SATURN clinical trial report. It commented that the patients in the SATURN trial received a variety of post-progression

treatments, many of which are not routinely used in the UK (including pemetrexed, vinorelbine, gemcitabine and paclitaxel). Only docetaxel and erlotinib are recommended by NICE for second-line treatment of non-small-cell lung cancer. The ERG noted that this was likely to affect overall survival results. It commented that the clinical evidence for erlotinib in patients with stable disease was based on a post hoc unstratified subgroup analysis and that the evidence for patients with squamous and non-squamous disease came from a further post hoc division of this subgroup, again according to an unstratified variable. The ERG considered that the SATURN trial was not designed to perform these types of analyses and therefore the results should be interpreted with caution.

3.22 The ERG identified data on patients with stable, non-squamous disease from the JMEN trial. It was therefore able to carry out an indirect comparison of pemetrexed and erlotinib (using data from the SATURN trial) for this patient group. The results indicated a statistically significant progression-free survival benefit for pemetrexed (HR 0.64; 95% CI 0.47 to 0.89) but the difference was not statistically significant for overall survival (HR 0.93; 95% CI 0.66 to 1.30). However, the ERG considered that the results of this analysis should be interpreted with caution because of differences in the patient populations in the JMEN and SATURN studies, the limitations of using post hoc subgroup analyses, and the uncertainty about whether both studies could be generalised to patients in the UK.

3.23 The ERG reviewed the economic analyses originally submitted by the manufacturer and the additional analyses provided in response to consultation on both appraisal consultation documents. It considered that the comparison of erlotinib with best supportive care in the total population of patients with stable disease could be misleading because it could mask differences in clinical and cost effectiveness between the squamous and non-squamous disease groups. In addition, the ERG considered that results from the SATURN trial suggest that following disease progression, subsequent survival rates differ between patients with squamous and non-squamous disease, as there appears to be no difference in post-progression survival in the non-squamous disease group, whereas approximately 60% of the survival benefit associated with erlotinib maintenance treatment occurs during the post-progression period in the squamous disease group. In addition, there was statistically significant heterogeneity in some of the prognostic factors of the patients with squamous and non-squamous disease in

the SATURN trial. Therefore, the ERG expressed the view that it was not appropriate to combine the histological groups and hence did not conduct any sensitivity analyses on the manufacturer's estimates for the total stable disease population.

3.24 The ERG's main criticism of the models of erlotinib compared with best supportive care in the subgroups of patients with squamous and non-squamous disease was the method used to extrapolate survival beyond the trial period. It noted that the manufacturer had not used post-progression survival data directly from the trial, but instead calculated post-progression survival as the difference between overall survival and progression-free survival. The ERG commented that because all patients in the stable disease population of the SATURN trial had disease which had progressed (that is, the progression-free survival data set was complete), there was no need to model the mean duration of progression-free survival because it could be based directly on Kaplan-Meier survival estimates from the trial. The ERG estimated mean overall survival using new survival data provided by the manufacturer during consultation on the first appraisal consultation document, by adding progression-free survival to post-progression survival and adjusting the estimate to exclude patients dying at or before disease progression. For post-progression survival in the subgroup of patients with squamous disease, the ERG used Kaplan-Meier estimates up to a 20% survival figure and then modelled the remaining survival. For the subgroup of patients with non-squamous disease, data on post-progression survival were available up to 600 days, but required modelling after this point for the remaining 7% of patients; a common exponential model was used for both the intervention and the comparator. The ERG's approach to modelling survival resulted in mean overall survival gains of 3.4 months (95% CI 1.5 to 5.3 months) for patients with stable, squamous disease and 2.2 months (95% CI 0.9 to 3.5 months) for patients with stable, non-squamous disease (corresponding to a 28% and 75% decrease in QALY gains compared with those in the manufacturer's base case respectively). The ERG stressed the wide confidence intervals around these estimates of survival gain. For the population of patients with stable, squamous disease the manufacturer's base-case ICER for erlotinib compared with best supportive care increased from £35,491 to £44,812 per QALY gained (incremental cost £7,129, incremental benefit 0.1591 QALYs) using the ERG's modelling approach. For the population of patients with stable, non-squamous disease the manufacturer's base-case ICER for erlotinib compared with best supportive care

increased from £40,020 to £68,120 per QALY gained (incremental cost £8,340, incremental benefit 0.1224 QALYs).

3.25 The ERG commented on the manufacturer's economic analysis of erlotinib compared with pemetrexed in the population of patients with stable, non-squamous disease. It noted that the manufacturer's estimate of pemetrexed costs did not account for gender differences in body surface area. It also noted that a modifying factor that reduced pemetrexed costs by 5% had been used and that no evidence had been provided to support this method. The ERG revised the manufacturer's model using their own estimation of pemetrexed costs, and used the hazard ratios from its indirect analysis (noting the previously mentioned caution about this analysis). The resulting ICER was based on the lower costs (-£8,460) and lower efficacy (-0.1007 QALYs) of erlotinib compared with pemetrexed and represented a cost saving of £84,029 per QALY lost.

3.26 Full details of all the evidence are in the manufacturer's submission and the ERG report.

Consideration of the evidence

3.27 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of maintenance treatment with erlotinib, having considered evidence on the nature of non-small-cell lung cancer and the value placed on the benefits of erlotinib by people with the condition, those who represent them, and clinical specialists. It also took into account the effective use of NHS resources and comments received during consultation on both appraisal consultation documents.

3.28 The Committee considered current UK practice for the treatment of patients with locally advanced or metastatic non-small-cell lung cancer. It heard from clinical specialists that first-line treatment in the UK is usually with carboplatin or cisplatin plus gemcitabine or vinorelbine, or cisplatin plus pemetrexed for patients with non-squamous disease. If disease progresses, patients have the option of receiving second-line systemic treatment if they have a good performance status. In the UK, second-line treatment is normally docetaxel or erlotinib. The Committee was aware that maintenance treatment after first-line treatment is still

a relatively new concept in lung cancer and that its aim is to prolong the benefits of first-line treatment and to maximise quality of life for as long as possible. It noted that best supportive care is currently the only maintenance treatment option for patients with squamous disease. However, pemetrexed is recommended in NICE's technology appraisal guidance on pemetrexed for the maintenance treatment of non-small-cell lung cancer as an option for the maintenance treatment of people with locally advanced or metastatic non-small-cell lung cancer other than predominantly squamous cell histology if disease has not progressed immediately following platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel. The Committee noted that patients are only eligible for maintenance treatment with pemetrexed if they have not received it as part of first-line treatment in combination with cisplatin. It heard from clinical specialists that the number of patients who would be eligible for maintenance treatment with pemetrexed is already small and would progressively decrease as more patients receive first-line treatment with pemetrexed (in line with NICE's technology appraisal guidance on pemetrexed for the first-line treatment of non-small-cell lung cancer).

3.29 The Committee noted views from the clinical specialists that erlotinib is an oral drug with adverse effects that are well known and relatively well tolerated. The clinical specialists stated that a potential benefit of maintenance treatment is that it may keep some patients well enough to be able to receive subsequent treatment after first-line therapy. The clinical specialists also commented that erlotinib may provide a maintenance treatment option for patients who cannot receive pemetrexed maintenance treatment because they have squamous disease and/or they have had pemetrexed as a first-line treatment. The Committee also noted a statement from a patient group which emphasised that even relatively small improvements in survival and quality of life afforded by new treatments compared with current treatment options is of real importance to patients.

Clinical effectiveness

3.30 The Committee discussed the evidence on the clinical effectiveness of erlotinib for the maintenance treatment of patients with stable disease. It noted that 1 randomised trial, the SATURN trial, was presented, which showed that

maintenance treatment with erlotinib was associated with a statistically significant improvement in progression-free survival and overall survival compared with placebo for the overall population of patients with stable disease. It noted that the improvement in progression-free survival with erlotinib was similar for patients in the squamous and non-squamous disease subgroups, but a statistically significant improvement in overall survival was only demonstrated in the subgroup of patients with squamous disease (HR 0.67; 95% CI 0.48 to 0.92 compared with HR 0.76; 95% CI 0.59 to 1.00 in the non-squamous disease group). The Committee was aware that the results for patients with stable disease were based on a post hoc subgroup analysis of 55% of the SATURN trial population. Furthermore, the results for the subgroups of patients with squamous and non-squamous disease were also post hoc analyses based on a disaggregation of the stable disease population and there were relatively small numbers of patients in each subgroup (190 and 297 respectively). The Committee was aware that the SATURN trial had not been designed for such analyses. It therefore regarded that the true magnitude of the benefits of erlotinib in these patient populations was uncertain. The Committee considered that the adverse events associated with erlotinib (most commonly, rash and diarrhoea) were well known and noted that most patients in the SATURN trial did not require their treatment to be changed or stopped because of adverse events.

3.31 The Committee discussed whether the results of the SATURN trial could be generalised to UK clinical practice, noting that in the trial there were few UK patients, a high proportion of south-east Asian patients and a high proportion of patients who had never smoked. The Committee was aware that Asian patients are known to respond better to lung cancer treatments than patients of other races and patients who have never smoked respond better than those with a history of smoking. It also noted that in the SATURN trial 30% of patients with stable disease still had an ECOG performance status of 0 after 4 cycles of chemotherapy and this was likely to reflect a fitter group of patients than the population who would receive maintenance treatment with erlotinib in UK clinical practice. The Committee also observed that 66% of patients in the SATURN trial were under 65 years of age and represented a younger population of patients with non-small-cell lung cancer than would be seen in UK clinical practice. It also noted that a high proportion of patients went on to receive further systemic therapy after the SATURN trial, some of which is not routinely given to patients in UK clinical practice. The Committee therefore concluded that the results from the

SATURN trial had limited generalisability to UK clinical practice, therefore adding further uncertainty to the true magnitude of the benefits of erlotinib that would be achieved for UK patients.

3.32 The Committee acknowledged that the manufacturer provided updated analyses for the stable, non-squamous disease group, during consultation on the appraisal consultation documents, which adjusted for some prognostic factors (ECOG status and smoking history), which the manufacturer suggested may have biased results against erlotinib in the SATURN trial. However, the Committee was concerned about the reliability of the data because of the small numbers of patients included in these further subgroup analyses. The Committee heard from the ERG that the differences in ECOG status and smoking history between the erlotinib and best supportive care groups were not statistically significant in the non-squamous disease population and that the differences in these baseline characteristics would not artificially decrease the overall survival estimate for erlotinib. The Committee also acknowledged comments from the ERG that no adjustments for other prognostic factors that could have had an impact on overall survival, such as gender and disease stage, had been made in these analyses by the manufacturer. The Committee further heard from the ERG that in a previous trial, patients with non-squamous disease experienced an additional gain in overall survival when treated with first-line pemetrexed and cisplatin compared to other chemotherapy regimens. In the light of these findings, it is unclear whether erlotinib maintenance treatment will supplement the extended survival advantage seen when patients receive pemetrexed and cisplatin first-line chemotherapy, because no patients received pemetrexed plus cisplatin before the SATURN trial. The Committee therefore concluded that the manufacturer's adjusted estimates of overall survival for erlotinib compared with best supportive care for people with stable, non-squamous disease were associated with considerable uncertainty.

3.33 The Committee observed that all of the survival benefit for erlotinib compared with best supportive care in patients with non-squamous disease occurred in the progression-free period, however only 40% of survival benefit in patients with squamous disease was assumed to occur in the progression-free period. The Committee considered that there was no convincing explanation for the fact that most of the apparent survival benefit for erlotinib in the squamous disease group came after treatment had been discontinued. The Committee therefore regarded

the overall survival benefit for erlotinib in the squamous disease group with caution, agreeing that this estimate was highly uncertain.

3.34 The Committee was aware that EGFR mutation status was not recorded in half of the patients in the SATURN trial. It noted however that of the patients who were tested, a small proportion (11%) had activated EGFR mutations, and that this subgroup gained substantially more benefit from erlotinib than the trial population as a whole. It also heard from clinical specialists that these patients have a better prognosis with treatment than other patients with non-small-cell lung cancer. However, the Committee was aware that patients with EGFR mutations were unlikely to receive erlotinib maintenance treatment in UK clinical practice because NICE recommends gefitinib as an option for the first-line treatment in this group rather than chemotherapy (in NICE's technology appraisal guidance on gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer). The Committee was therefore concerned that some of the survival benefit of maintenance treatment with erlotinib demonstrated in the SATURN trial would not be seen in clinical practice because patients with EGFR mutations would usually receive gefitinib and would therefore not be eligible for maintenance treatment with erlotinib.

3.35 The Committee acknowledged that the manufacturer had provided additional information about the patient characteristics of the squamous disease population in the SATURN trial during consultation. The Committee accepted that these data showed that the number of patients with squamous disease with an activated EGFR mutation or who were of Asian origin or who had never smoked was small and therefore it agreed that these prognostic factors were unlikely to significantly bias the estimate of overall survival for this subpopulation. By implication, however, the Committee concluded that the numbers of patients with stable, non-squamous disease who had these baseline characteristics which may lead to better prognosis were even higher than previously thought.

3.36 The Committee discussed the first-line treatments received by patients in the SATURN trial. It considered that about 64% of patients received first-line chemotherapy regimens that are commonly used in the UK. The Committee noted that no 1 in the SATURN trial had received first-line treatment with pemetrexed and cisplatin, a regimen that is now commonly used as combination chemotherapy for patients with non-squamous disease because of its superiority

to the regimens used in the SATURN trial. The Committee considered that patients in the SATURN trial were fitter than patients seen in UK clinical practice, noting that patients with stable disease after 4 cycles of platinum-based chemotherapy still had a good performance status and approximately 60% of patients went on to receive further systemic therapy after the SATURN trial, some of which would not be routinely used in the UK. It also observed that only a small proportion of patients in the placebo group had received erlotinib after progression. It considered that the post-progression treatments and the small proportion of patients in the placebo group who had received erlotinib after progression would affect the estimates of overall survival in the erlotinib and placebo groups. The Committee was aware that it is unclear whether patients would benefit more from receiving erlotinib as maintenance treatment or for treatment of relapsed disease. The Committee concluded that there was very considerable uncertainty that the benefit of erlotinib seen in the trial would be translated into routine practice.

3.37 The Committee discussed the RECIST criteria for determining disease response in the SATURN trial, taking into account the marketing authorisation for erlotinib, which includes patients with stable disease only. It heard from clinical specialists that some centres, particularly those involved in clinical trials, use the RECIST criteria routinely but that centres less involved in research may not use RECIST criteria on a day-to-day basis. The Committee noted that the RECIST criteria used in the SATURN trial were based on 6-weekly CT scans and considered that such frequent scans were not likely in the routine care of lung cancer patients in the UK. The Committee therefore concluded that it was likely that the duration of erlotinib maintenance treatment in clinical practice would exceed that observed in the SATURN trial as CT scans would be performed less frequently.

3.38 In summary, the Committee agreed that the benefit of maintenance treatment with erlotinib seen in the SATURN trial was likely to be lower in routine clinical practice when considering that the trial population represented patients who are likely to have a better prognosis than the average patient treated in the UK. In addition, the Committee considered that there were several factors that led to considerable uncertainty about the magnitude of overall survival gain expected from erlotinib maintenance treatment in the stable population and in the squamous and non-squamous disease subpopulations. These included the small numbers of patients in the post hoc subgroup analyses informing the survival

estimates for the squamous and non-squamous disease groups and the use of post-progression treatments in the SATURN trial, which are not routinely used in the UK; and the lack of explanation as to why most of the survival benefit for erlotinib in the squamous disease group occurred after treatment was discontinued (in the post-progression period).

Cost effectiveness

3.39 The Committee was aware that a patient access scheme had been agreed between the manufacturer and the Department of Health. It noted that this is a simple scheme in which erlotinib is supplied to the NHS at a discount of 14.5% of the list price. The Committee concluded that it was appropriate to appraise the cost effectiveness of erlotinib maintenance treatment on the basis of ICERs that include this discount.

3.40 The Committee discussed the evidence for the cost effectiveness of erlotinib compared with best supportive care derived the manufacturer's new economic analyses provided during consultation on the first appraisal consultation document. The Committee noted that the costs used in the analyses were based on those used in previous NICE technology appraisals of treatments for non-small-cell lung cancer and considered them to be appropriate. The Committee noted the manufacturer's ICERs for erlotinib compared with best supportive care of £40,800 per QALY gained for all patients with stable disease, £35,500 per QALY gained for patients with stable, squamous disease, £40,000 per QALY gained for patients with stable, non-squamous disease. The Committee noted that the manufacturer's ICER for all patients with stable disease was greater than both the ICERs presented for the squamous and non-squamous groups and acknowledged that the factors that had the greatest effect on the manufacturer's new ICERs were assumptions about how much time a patient spent on treatment in the progression-free health state, and the costs attributed to best supportive care.

3.41 The Committee considered the ERG's critique of the manufacturer's economic analysis. It noted the ERG's comment that it was more appropriate to consider the cost effectiveness of erlotinib in the subgroups of patients with squamous disease and non-squamous disease separately, rather than in the stable disease

population as a whole, because of heterogeneity between the subgroups. The Committee agreed with the ERG, but was concerned about the subgroup analyses because the trial population had not been stratified by histology and analyses for these histological subgroups and for the stable disease population as a whole had not been predefined, which added uncertainty to the survival estimates and therefore also to the ICERs. Overall, the Committee concluded that it was justified in considering the squamous and non-squamous populations separately on clinical grounds.

3.42 The Committee discussed the ERG's comments on the methods used by the manufacturer to model progression-free survival and overall survival, in particular that post-progression survival had been calculated as the difference between overall survival and progression-free survival. The Committee concluded that the ERG's approach to estimating survival was more appropriate because it was based as much as possible on data directly from the trial and used modelling only when necessary. It noted that the ERG's modelling approach resulted in lower estimates of overall survival than the manufacturer's method, and that there were wide confidence intervals around these estimates, indicating a high degree of uncertainty. The Committee observed that the ERG's analyses resulted in significantly higher ICERs for erlotinib compared with best supportive care than those estimated by the manufacturer.

3.43 The Committee noted that the ERG's revisions to the manufacturer's model (including correcting the pemetrexed costs and using an alternative survival modelling method) increased the ICERs for erlotinib compared with best supportive care to £44,800 per QALY gained for treatment of stable, squamous disease and £68,100 per QALY gained for treatment of stable, non-squamous disease. The Committee considered that the most plausible ICERs would be considerably higher than those estimated by the ERG, and likely to be above £50,000 per QALY gained even for treatment of stable, non-squamous disease when taking into account the fact that the survival benefit observed in the SATURN trial was likely to be reduced in clinical practice where patients are less fit and have different prognostic characteristics from those seen in the trial population.

3.44 The Committee discussed the evidence for the cost effectiveness of erlotinib compared with pemetrexed. It noted that this was based on the manufacturer's

new economic analysis submitted in response to the first appraisal consultation document, in which various relative efficacy scenarios were modelled because of the lack of data for erlotinib compared directly with pemetrexed. The Committee was aware that erlotinib was less costly than pemetrexed. The Committee was aware that the manufacturer considered that the JMEN and SATURN trials were not directly comparable and that a robust estimate of the relative effectiveness of erlotinib and pemetrexed was not possible to establish. However, it noted that the ERG's indirect analysis of the JMEN and SATURN trials showed that erlotinib was less effective than pemetrexed. The Committee also observed the ERG's concerns not only about the comparability of these 2 trial populations but also about their generalisability to UK practice. In the light of these issues, the Committee concluded that it had not been presented with a plausible estimate of the cost savings per QALY lost that would be associated with the use of erlotinib maintenance compared with pemetrexed and that therefore, erlotinib could not be specifically recommended compared with pemetrexed.

3.45 The Committee noted the manufacturer's claim that pemetrexed maintenance treatment had been recommended in NICE's technology appraisal guidance on pemetrexed for the maintenance treatment of non-small-cell lung cancer for patients with non-squamous disease despite ICER estimates from the ERG exceeding £50,000 per QALY gained. However, the Committee understood that many considerations were taken into account by the Committee when finalising its appraisal of pemetrexed maintenance treatment, which subsequently decreased the ICER below £50,000 per QALY gained.

3.46 The Committee considered supplementary advice from NICE that should be taken into account when appraising treatments that may extend the life of patients with a short life expectancy and that are licensed for indications that affect small numbers of people with incurable illnesses. For this advice to be applied, all the following criteria must be met:

- The treatment is indicated for patients with a short life expectancy, normally less than 24 months.
- There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared with current NHS treatment.

The treatment is licensed or otherwise indicated for small patient populations. In addition, when taking these into account the Committee must be persuaded that the estimates of the extension to life are robust and the assumptions used in the reference case economic modelling are plausible, objective and robust.

3.47 The Committee noted that the median survival duration of patients in the UK with non-small-cell lung cancer who receive first-line chemotherapy is between 7 and 11 months. The Committee discussed the size of the patient population and was aware that the erlotinib marketing authorisation includes monotherapy for maintenance treatment of patients with locally advanced or metastatic non-small-cell lung cancer with stable disease after 4 cycles of standard platinum-based first-line chemotherapy, but also the treatment of patients with locally advanced or metastatic non-small-cell lung cancer after failure of at least 1 prior chemotherapy regimen. During consultation, the manufacturer estimated that about 4,100 patients would be suitable for treatment with erlotinib in the UK according to its current marketing authorisations. The Committee noted that the manufacturer had indicated that 6,700 patients receive first-line chemotherapy in the UK. Some of these patients would receive erlotinib as maintenance treatment rather than as a second-line therapy. The Committee also noted that the erlotinib marketing authorisation includes the treatment of patients with metastatic pancreatic cancer in combination with gemcitabine. Most of the 7,000 patients with pancreatic cancer present with metastatic disease and erlotinib would potentially be indicated for this population. The Committee discussed written evidence from a previous NICE technology appraisal appeal and noted that the Appeal Panel recognised that the criterion in the supplementary advice for end-of-life treatments for small patient populations indicated that 'Sufficient regard should be given to recognition of the desirability of developing new treatments in smaller disease areas and that higher prices, and therefore reduced cost effectiveness, were more likely to be justified given the need to recoup costs of development of the product from more limited licences'.The Appeal Panel had concluded that it was appropriate, according to the supplementary advice, to add together the potential patient populations covered by the marketing authorisation for different indications rather than on the basis of actual or recommended use. The Committee therefore considered that the true size of the cumulative population potentially eligible for treatment with erlotinib according to its UK marketing authorisations was not small and was considerably higher than the

manufacturer's estimate.

3.48 The Committee then discussed the extension to life offered by erlotinib for patients with stable disease. It also considered whether mean or median survival was a more appropriate measure for evaluating the end-of-life criteria. The Committee agreed with comments from the ERG that the mean survival figures were more informative because they were based on all available data for all patients across the whole trial period. The Committee also heard from the clinical specialists that some patients have significantly longer responses to treatment with erlotinib, which was another reason to consider the mean rather than the median values. It noted that in the new analyses provided during consultation, the manufacturer estimated the mean overall survival benefit of erlotinib compared with best supportive care to be 3.3 months in the whole stable disease population, 4.2 months in the stable, squamous disease population and 4.5 months in the stable, non-squamous disease population. It also noted that the ERG estimated the mean overall survival benefit to be 3.4 months and 2.2 months in the populations of patients with squamous and non-squamous disease respectively. The Committee was concerned that no rationale could be provided to explain why both the manufacturer's median and mean survival estimates for each subpopulation were greater than for the whole population, which cast uncertainty over the validity of the analysis. During consultation the manufacturer explained that this was because of the different prognostic baseline characteristics of the patients in the squamous and non-squamous disease groups. Although the ERG did not provide an overall survival estimate for the whole stable disease population, the Committee heard from the ERG that this figure was likely to be closer to the mean overall survival estimate for patients in the non-squamous disease group (that is, 2.2 months) than the mean overall survival estimate for patients in the squamous disease group (that is, 3.4 months). The Committee had previously concluded that the overall survival benefit of erlotinib in clinical practice was uncertain and likely to be less than the ERG's estimates. The Committee did not consider that robust evidence had been provided to demonstrate an extension to life of at least 3 months and, taken together with the consideration on population size, therefore concluded that the end-of-life criteria were not met in this appraisal.

3.49 In summary, the Committee considered that the most plausible ICERs for erlotinib compared with best supportive care would be higher than those estimated by the

ERG (£44,800 and £68,100 per QALY gained for treatment of patients with stable, squamous disease and with stable, non-squamous disease respectively) and considerably above £50,000 per QALY gained for treatment of the whole stable disease population. The Committee agreed that the end-of-life criteria were not met in this appraisal, but it noted that even if they were taken into account, the most plausible ICERs were higher than those normally considered to be associated with cost effective treatments. The Committee concluded that erlotinib was likely to be associated with cost savings per QALY lost compared with pemetrexed in patients with stable, non-squamous disease, but that it was not possible to establish a robust estimate. It therefore agreed that no specific recommendation could be made related to the use of erlotinib compared with pemetrexed. The Committee concluded that erlotinib could not be considered a cost-effective use of NHS resources when used as monotherapy for maintenance treatment in patients with locally advanced or metastatic non-small-cell lung cancer who have stable disease following platinum-based first-line chemotherapy.

3.50 The Committee discussed whether NICE's duties under the equalities legislation required it to alter or add to its recommendations in any way. It noted that in response to the second appraisal consultation document the manufacturer stated that the preliminary recommendations mean that patients with squamous disease will not have a maintenance treatment option, whereas those with non-squamous disease currently have access to pemetrexed maintenance treatment through NICE's technology appraisal guidance on pemetrexed for the maintenance treatment of non-small-cell lung cancer. The manufacturer further stated that the histological mix of non-small-cell lung cancer shows a gender imbalance with squamous disease making up a substantially larger proportion of non-small-cell lung cancer in men. It was the manufacturer's view therefore that having no maintenance treatment option for people with squamous disease has a greater impact on men with non-small-cell lung cancer, and that this was particularly concerning given that men have an inherently worse prognosis than women. The Committee noted that no data on gender distribution based on histology were provided by the manufacturer and therefore this assertion was impossible to substantiate. However, the Committee noted that any possible differences in maintenance treatment access referred to by the manufacturer were related to NICE's technology appraisal guidance on pemetrexed for the maintenance treatment of non-small-cell lung cancer, rather than this appraisal. The

Committee agreed that its decision about erlotinib maintenance treatment needed to be based on the evidence seen in this appraisal. Furthermore, the final decision not to recommend erlotinib maintenance treatment was made because erlotinib was not cost-effective in either of the squamous or non-squamous subgroups compared with best supportive care. The Committee concluded that its recommendations do not make it more difficult in practice for a specific group to access erlotinib maintenance treatment compared with other groups. In addition, the Committee noted that, following the publication of NICE's technology appraisal guidance on pemetrexed for the first-line treatment of non-small-cell lung cancer, the proportion of patients who would be eligible to receive pemetrexed maintenance treatment was declining quickly over time (because they are receiving pemetrexed as a first-line treatment instead) and therefore the manufacturer's concern that pemetrexed is currently only available as a maintenance option for non-squamous disease was becoming less relevant.

4 Appraisal Committee members and NICE project team

Appraisal Committee members

The Appraisal Committees are standing advisory committees of NICE. Members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. There are 4 Appraisal Committees, each with a chair and vice chair. Each Appraisal Committee meets once a month, except in December when there are no meetings. Each Committee considers its own list of technologies, and ongoing topics are not moved between Committees.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Dr Darren Ashcroft
Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester

Dr Matthew Bradley
Value Demonstration Director, AstraZeneca

Dr Brian Buckley
Lay Member

Professor Usha Chakravarthy
Professor of Ophthalmology and Vision Sciences, Queen's University of Belfast

Professor Peter Clark (Chair)
Consultant Medical Oncologist, Clatterbridge Centre for Oncology

Dr Ian Davidson
Lecturer in Rehabilitation, University of Manchester

Professor Simon Dixon
Professor of Health Economics, University of Sheffield

Dr Martin Duerden
Medical Director, Conwy Local Health Board

Dr Alexander Dyker
Consultant Physician, Wolfson Unit of Clinical Pharmacology

Gillian Ells
Prescribing Advisor, NHS Sussex Downs and Weald

Dr Jon Fear
Consultant in Public Health Medicine, Head of Healthcare Effectiveness NHS Leeds

Paula Ghaneh
Senior Lecturer and Honorary Consultant, University of Liverpool

Niru Goenka
Consultant Physician, Countess of Chester NHS Foundation Trust

Professor Carol Haigh
Professor in Nursing, Manchester Metropolitan University

Alison Hawdale
Lay Member

Professor John Hutton
Professor of Health Economics, University of York

Professor Peter Jones
Pro Vice Chancellor for Research and Enterprise, Keele University

Professor Peter Jones
Pro Vice Chancellor for Research and Enterprise, Keele University; Professor of Statistics,

Keele University

Dr Steven Julious
Senior Lecturer in Medical Statistics, University of Sheffield

Dr Vincent Kirkbride
Consultant Neonatologist, Regional Neonatal Intensive Care Unit, Sheffield

Dr Rachel Lewis
Doctoral Researcher, Manchester Business School

Dr Anne McCune
Consultant Hepatologist, University Hospitals Bristol NHS Foundation Trust

Professor Jonathan Michaels (Vice Chair)
Professor of Vascular Surgery, University of Sheffield

Dr Neil Milner
General Medical Practitioner, Tramways Medical Centre

Professor Oluwafemi Oyebode
Professor of Psychiatry and Consultant Psychiatrist, The National Centre for Mental Health

Mr Mike Pinkerton
Chief of Business Development, The Rotherham NHS Foundation Trust

Dr John Radford
Director of Public Health, Rotherham Primary Care Trust

Dr Phillip Rutledge
GP and Consultant in Medicines Management, NHS Lothian

Dr Brian Shine
Consultant Chemical Pathologist, John Radcliffe Hospital

Dr Murray D Smith
Associate Professor in Social Research in Medicines and Health, University of Nottingham

Mr Paddy Storrie
Lay Member

Dr Cathryn Patricia Thomas
GP and Associate Professor, University of Birmingham

Charles Waddicor
Chief Executive, NHS Berkshire

Mr Mike Wallace
Health Economics and Reimbursement Director, Johnson and Johnson Medical Ltd

Dr Lok Yap
Consultant in Acute Medicine and Clinical Pharmacology, Whittington Hospitals NHS Trust

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Helen Tucker and Sally Gallaugher
Technical Leads

Fiona Rinaldi
Technical Adviser

Kate Moore
Project Manager

Sources of evidence considered by the Committee

The Evidence Review Group (ERG) report for this appraisal was prepared by Liverpool Reviews and Implementation Group (LRIG):

- Bagust A, Boland A, Blundell M et al. Erlotinib monotherapy for the maintenance treatment of non-small cell lung cancer after previous platinum-containing therapy,

March 2010

The following organisations accepted the invitation to participate in this appraisal as consultees and commentators. They were invited to comment on the draft scope, the ERG report and the appraisal consultation document (ACD). Manufacturers or sponsors were also invited to make written submissions. Professional or specialist, patient or carer groups, and other consultees, had the opportunity to give their expert views. Manufacturers or sponsors, professional or specialist, patient or carer groups, and other consultees, also have the opportunity to appeal against the final appraisal determination.

Manufacturers or sponsors:

- Roche Products

Professional or specialist, and patient or carer groups:

- Macmillan Cancer Support
- Roy Castle Lung Cancer Foundation
- British Thoracic Society
- National Lung Cancer Forum for Nurses
- Royal College of Nursing
- Royal College of Physicians' Intercollegiate Lung Cancer Group
- United Kingdom Oncology Nursing Society

Other consultees:

- NHS Cornwall and the Isles of Scilly
- Department of Health
- NHS Dudley
- Welsh Assembly Government

Commentator organisations (did not provide written evidence and without the right of appeal):

- NHS Quality Improvement Scotland
- Eli Lilly and Company
- British Thoracic Oncology Group
- Liverpool Reviews and Implementation Group (LRIG)
- National Institute for Health Research Health Technology Assessment Programme
- National Collaborating Centre for Cancer

The following individuals were selected from clinical specialist and patient expert nominations from the non-manufacturer or sponsor consultees and commentators. They gave their expert personal view on erlotinib by attending the initial Committee discussion and providing written evidence to the Committee. They were also invited to comment on the ACD.

- Professor David Ferry, Consultant Medical Oncologist, nominated by Eli Lilly and Company – clinical specialist
- Dr Diane Parry, Consultant Physician and Lung Cancer Lead, nominated by Welsh Assembly Government – clinical specialist
- Dr Yvonne Summers, Honorary Lecturer, nominated by Royal College of Physicians – clinical specialist
- Dr Clive Mulatero, Senior Lecturer in Medical Oncology, nominated by Royal College of Physicians – clinical specialist

The following individuals were nominated as NHS Commissioning experts by the selected PCT allocated to this appraisal. They gave their expert and NHS commissioning personal view on erlotinib by attending the initial Committee discussion and providing written evidence to the Committee. They were also invited to comment on the ACD.

- Dr Caroline Court, Consultant in Public Health Medicine and Public Health Lead for Cancer, NHS Cornwall, selected by NHS Cornwall and Isles of Scilly – NHS Commissioning expert

Representatives from the following manufacturer or sponsor attended Committee Meetings. They contributed only when asked by the Committee chair to clarify specific issues and comment on factual accuracy.

- Roche Products

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