NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Dacomitinib for untreated EGFR mutation-positive non-small-cell lung cancer

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using dacomitinib in the NHS in England. he appraisal committee has considered the evidence submitted and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the committee papers).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: April 2019

Note that this document is not NICE's final guidance on dacomitinib. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using dacomitinib in the NHS in England.

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 9 May 2019

Second appraisal committee meeting: 23 May 2019

Details of membership of the appraisal committee are given in section 5.

1 Recommendations

1.1 Dacomitinib is not recommended, within its marketing authorisation, for untreated locally advanced or metastatic epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer (NSCLC) in adults.

1.2 This recommendation is not intended to affect treatment with dacomitinib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Locally advanced or metastatic EGFR mutation-positive NSCLC is usually first treated with afatinib, erlotinib or gefitinib.

Evidence from a randomised controlled trial suggests that people who take dacomitinib live longer than people who take gefitinib. They also live longer before their disease gets worse. But there is no direct evidence comparing dacomitinib with afatinib, which may be more effective than erlotinib and gefitinib.

There is also uncertainty about the assumptions used in the cost-effectiveness modelling, including about utility values, the treatments used after disease progression, how survival has been extrapolated and the results of the indirect comparisons.

Dacomitinib does not meet NICE's criteria to be considered a life-extending treatment at the end of life. It also does not meet NICE's criteria to be included in the Cancer Drugs Fund. The most plausible cost-effectiveness estimates are above what NICE normally considers an acceptable use of NHS resources. So dacomitinib is not recommended.

2 Information about dacomitinib

Anticipated marketing authorisation indication	On 31 January 2019, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product dacomitinib (Vizimpro, Pfizer), intended for the first-line treatment of adult patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations.
Dosage in the marketing authorisation	Based on the company submission, dacomitinib is given orally at a dosage of 45 mg until disease progression or unacceptable toxicity. Dacomitinib is available in 3 dose strengths: 45 mg, 30 mg and 15 mg.
Price	The price was submitted as commercial in confidence. The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Pfizer and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

Clinical need

People would welcome a new treatment option

3.1 The patient experts highlighted that epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer (NSCLC) tends to present late, so people have more advanced disease at diagnosis compared with the wider NSCLC population. The patient experts also noted that dacomitinib may improve overall survival, which is especially important to patients and their families. The committee agreed that people

with EGFR mutation-positive NSCLC would welcome additional treatment options that improve overall survival.

Clinical management

Erlotinib, gefitinib and afatinib are appropriate comparators

3.2 The clinical experts explained that in line with NICE guidance, locally advanced or metastatic EGFR mutation-positive NSCLC is usually first treated with a tyrosine kinase inhibitor such as erlotinib, gefitinib or afatinib. The committee understood that afatinib is more common in NHS clinical practice in England because as a second-generation tyrosine kinase inhibitor it is better than both erlotinib and gefitinib (first-generation tyrosine kinase inhibitors) in terms of prolonging progression-free survival. The committee also understood that afatinib is associated with more adverse events than erlotinib and gefitinib, so it is generally only offered to people with good Eastern Cooperative Oncology Group (ECOG) performance status. The clinical experts explained that this would also be the case for dacomitinib. The committee agreed that although afatinib is the most commonly used tyrosine kinase inhibitor and has a similar adverse-event profile to dacomitinib, gefitinib and erlotinib were also used in established NHS practice in England and so were listed as comparators in the final scope issued by NICE.

Clinical evidence

Evidence from an open-label randomised controlled trial is relevant and high quality

3.3 The main clinical evidence came from ARCHER 1050, a multicentre, open-label, phase III randomised controlled trial. It compared the efficacy and safety of dacomitinib (n=227) with gefitinib (n=225) in adults with untreated locally advanced or metastatic EGFR mutation-positive NSCLC (patients had either the exon 19 deletion or exon 21 [L858R] EGFR mutations). The trial included 71 study sites in 7 countries (China, Hong

Kong, Japan, Republic of Korea, Italy, Poland and Spain). The primary outcome was progression-free survival, determined by blinded independent review committee. Secondary outcomes included overall survival, objective response rate, length of response, adverse events, time to treatment failure and health-related quality of life. After disease progression, patients could have subsequent treatment with a different drug (see section 3.6). The committee noted that in the trials used to inform NICE technology appraisal guidance on erlotinib, gefitinib and afatinib, the comparator was chemotherapy, whereas in ARCHER 1050 the comparator was gefitinib (that is, the trial compared a second-generation tyrosine kinase inhibitor [dacomitinib] with a first-generation tyrosine kinase inhibitor [gefitinib]). The committee concluded that ARCHER 1050 was a well conducted trial which provided high-quality evidence that was relevant to the appraisal.

The treatment arms in ARCHER 1050 are well balanced

3.4 The ERG noted that in the trial, 64.3% of patients having dacomitinib were women compared with only 55.6% of patients having gefitinib. The committee was aware that there was some evidence to suggest that tyrosine kinase inhibitors tend to be more effective at treating EGFR mutation-positive NSCLC in women than in men, and so the trial could be biased in favour of dacomitinib. But the clinical experts did not consider sex to be an important factor. The committee concluded that the treatment arms in ARCHER 1050 were generally well balanced.

Dacomitinib improves progression-free and overall survival compared with gefitinib

3.5 The results of ARCHER 1050 showed that dacomitinib statistically significantly improved progression-free survival compared with gefitinib (14.7 months for dacomitinib compared with 9.2 months for gefitinib; hazard ratio 0.589, 95% confidence interval [CI] 0.47 to 0.74). The results also showed that dacomitinib statistically significantly improved overall survival compared with gefitinib (34.1 months for dacomitinib compared

with 26.8 months for gefitinib; hazard ratio 0.760, 95% CI 0.58 to 0.99). The committee concluded that dacomitinib is associated with improved progression-free and overall survival compared with gefitinib.

It is unclear how subsequent treatments may affect overall survival in ARCHER 1050

3.6 In ARCHER 1050, patients who stopped taking the study drug (dacomitinib or gefitinib) could then have subsequent treatment with a different drug (the company considered the drugs used as subsequent treatments to be confidential so they cannot be reported here). But the committee noted that these subsequent treatments did not reflect the type and proportion of those used in clinical practice in the NHS in England. The committee agreed that there was uncertainty about how subsequent treatments may have affected the overall survival estimates in ARCHER 1050, and that it would consider this in its decision making.

The results of ARCHER 1050 are generalisable to NHS clinical practice in England

3.7 The committee considered whether the baseline characteristics of patients in ARCHER 1050 reflected those seen in NHS clinical practice in England. It noted that the patients in the trial had only the exon 19 deletion (del19) or exon 21 (L858R) EGFR mutations. The clinical experts explained that these 2 mutations account for around 90% of all EGFR mutations. Moreover, most trials only include people with these mutations, and they were the same mutations that were included in clinical trials of other tyrosine kinase inhibitors. The committee acknowledged that although other mutations may respond less well to dacomitinib, the Committee for Medicinal Products for Human Use (CHMP) did not restrict its positive opinion for dacomitinib to these 2 mutations (see table 2). It therefore agreed that the EGFR mutation status of patients in ARCHER 1050 generally reflected those seen in NHS clinical practice in England. The committee also noted that the trial included a large proportion of patients of Asian family origin (74.9% in the dacomitinib treatment arm and 78.2%

in the gefitinib treatment arm) because many of the trial centres were in East Asia. It recalled that ethnicity was a prespecified subgroup in ARCHER 1050, and that the company had provided analyses in response to clarification but the results were underpowered (the results are considered academic in confidence by the company and so cannot be reported here). Given the subgroup analyses' lack of robustness, the committee considered that the results from the whole trial population would be generalisable to the population seen in clinical practice in England. The committee noted that ARCHER 1050 excluded people with brain metastases: these are associated with a poor prognosis and often occur in people with EGFR mutation-positive NSCLC. This was an important difference between ARCHER 1050 and the LUX-Lung 7 trial (used in the comparison of afatinib with gefitinib; see section 3.9), in which 16% of patients had brain metastases. The committee concluded that overall, the trial results from ARCHER 10150 were generalisable to NHS clinical practice in England.

Dacomitinib is associated with more adverse events and may need more dose reductions than gefitinib

3.8 The committee noted that dacomitinib had a higher incidence of common adverse events than gefitinib, and that there were more dose reductions in the dacomitinib treatment arm than in the gefitinib treatment arm (66.1% and 8.0% respectively). The committee was also aware that second-generation tyrosine kinase inhibitors such as afatinib are associated with more adverse events, whereas first-generation tyrosine kinase inhibitors are generally better tolerated (see section 3.2). The clinical experts agreed that the differences in the drugs' adverse-event profiles are well known and this is reflected in how they are used in clinical practice (that is, according to a person's fitness for treatment, which is typically categorised by ECOG performance status). Although the clinical experts acknowledged that adverse events associated with second-generation tyrosine kinase inhibitors could be effectively managed in clinical practice,

they highlighted that the adverse events were detrimental to people's quality of life. The clinical lead for the Cancer Drugs Fund also highlighted NHS England's concerns about the toxicity of dacomitinib and the high rates of adverse events that are likely to be seen in practice. The committee agreed that dacomitinib had a higher incidence of adverse events and needed more dose reductions than gefitinib. It concluded that how this affected health-related quality of life and resource costs for managing adverse events should be fully captured in the cost-effectiveness analysis.

The results from the company's fractional polynomial network meta-analysis are uncertain

3.9 The company did a network meta-analysis to compare dacomitinib with the other comparators in the scope, afatinib and erlotinib. It did a fractional polynomial network meta-analysis as described by Janssen et al. (2011), because it considered that the proportional hazards assumption may have been violated in ARCHER 1050 (that is, the hazard ratios were not constant over time). The committee understood that fractional polynomial network meta-analysis differs from a traditional network meta-analysis in that it fits hazard ratios that can vary over time rather than being constant. Based on the evidence from clinical experts, other phase III randomised controlled trials and previous NICE appraisals, the company assumed equivalence between gefitinib and erlotinib. The committee agreed that this assumption was appropriate. The company obtained the relative effect estimates of progression-free and overall survival for afatinib and dacomitinib compared with gefitinib from the LUX-Lung 7 trial (which compared afatinib with gefitinib). In its submission, the company had presented the projected means for progression-free and overall survival along with the medians compared with the observed data from ARCHER 1050, to provide face validity for model (the company considered the results to be commercial in confidence and so they cannot be reported here). The committee recalled the ERG's concerns about differences in

patients' baseline characteristics in ARCHER 1050 and LUX-Lung 7, specifically the proportion of patients of Asian family origin and the presence of brain metastases (see section 3.7). The committee agreed that these differences, in particular the exclusion of brain metastases from ARCHER 1050, added uncertainty to any estimates from the analysis. The ERG also expressed concerns about extrapolating progression-free and overall survival outcomes from fractional polynomial models: they tend to over-fit to the tail of the data, often resulting in implausible survival extrapolations. The committee noted that these concerns were supported by the large number of models that the company had to reject because of the clinically implausible extrapolations of survival outcomes. The committee concluded that the results from the company's fractional polynomial network meta-analysis were uncertain.

There is no statistically significant difference between dacomitinib and afatinib in terms of progression-free and overall survival

3.10 The ERG did its own indirect treatment comparison to address these uncertainties, and because the company's model did not report hazard ratios for progression-free or overall survival between dacomitinib and afatinib. The ERG did a fixed-effects network meta-analysis using data from ARCHER 1050 for dacomitinib and from LUX-Lung 7 for afatinib. The company agreed with the ERG's approach to estimating the hazard ratios. The results suggested that dacomitinib might be better than afatinib in terms of extending progression-free and overall survival, but there was no significant difference between the 2 treatments (progression-free survival hazard ratio 0.80, 95% CI 0.57 to 1.12; overall survival hazard ratio 0.88, 95% CI 0.61 to 1.29). The committee recalled that there was uncertainty around any estimates from a network meta-analysis that used data from ARCHER 1050 and LUX-Lung 7, because of the differences between the trials in terms of baseline patient characteristics (and because the proportional hazards assumption may have been violated in ARCHER 1050). It concluded that any estimates were uncertain and based on the

evidence available there was no statistically significant difference between dacomitinib and afatinib in terms of extending progression-free and overall survival.

The company's economic model

The company's model is appropriate for decision making

3.11 The company used a partitioned-survival economic model that included 3 health states: pre-progression, post-progression and death. The committee concluded that the model was generally appropriate and consistent with the models used in other appraisals for NSCLC. The model included either dacomitinib, afatinib, gefitinib or erlotinib as first-line treatment, followed by osimertinib (if T790M mutation positive) or chemotherapy. The committee was concerned that the model captured only the costs and not the clinical benefits of subsequent treatments.

Survival extrapolation

There are uncertainties in how the company modelled progression-free survival

3.12 In its base case, the company modelled progression-free survival for gefitinib using a generalised gamma curve fitted to the gefitinib treatment arm of ARCHER 1050. It modelled progression-free survival for erlotinib by assuming equivalent efficacy with gefitinib. It then used the fractional polynomial network meta-analysis (model P1=0.5, P2=1.5) to obtain time-varying hazard ratios for afatinib and dacomitinib relative to gefitinib (see section 3.10), before applying these to the gefitinib extrapolation. The committee had concerns about the company's modelling of progression-free survival:

- The progression-free survival for gefitinib after 2 years potentially underestimated the quality-adjusted life years (QALYs) and costs for the comparators.

- The extrapolation of dacomitinib and afatinib was reliant on results from the fractional polynomial network meta-analysis, which were themselves uncertain (see section 3.9).
- The progression-free survival curves suggested that dacomitinib had the highest progression-free survival until 38 months, beyond which afatinib had the highest progression-free survival. The committee agreed that there was no clinical rationale for dacomitinib to be less effective than the comparators in terms of progression-free survival after 38 months.

The committee agreed that there was uncertainty around the company's modelling of progression-free survival because of the implausibility of the results and this made the company's ICERs highly uncertain.

The ERG's modelling of progression-free survival is appropriate

3.13 In its base case, the ERG used the log-normal parametric curve for gefitinib and the fractional polynomial network meta-analysis for the other comparators (P1=0.5, P2=1). The afatinib extrapolation remained implausible so the ERG assumed the progression-free survival of afatinib to be equal to the mean progression-free survival of dacomitinib and gefitinib after 36 months. It also did a scenario analysis in which it assumed the progression-free survival of afatinib to be equal to the mean progression-free survival of dacomitinib and gefitinib after 55 months. Although it recognised the uncertainties, the committee preferred this approach because it produced more plausible results than the company's base case. It therefore agreed that the ERG's modelling of progression-free survival was appropriate and should form the basis of its decision making.

The company's modelling of overall survival produces some implausible results

3.14 In its base case, the company modelled overall survival in the same way it modelled progression-free survival (see section 3.12). The committee had concerns about the company's modelling of overall survival:

- The generalised gamma curve may underestimate overall survival with gefitinib.
- The modelling suggested that the efficacy of afatinib relative to gefitinib decreased over time while the efficacy of dacomitinib improved over time; clinical expert advice to the ERG questioned the plausibility of this. The clinical experts acknowledged that effective treatments may provide some benefit for a limited time after stopping treatment, but the committee recalled that there was no evidence to suggest that afatinib and dacomitinib provided different benefits after stopping treatment.
- Dacomitinib appears to provide benefits both before and after disease progression. This is unlikely to be plausible, because it is uncommon for progression-free survival to mirror post-progression survival, and even less common for progression-free survival to be extended into post-progression survival.

The committee therefore agreed that the company's modelling of overall survival produced some implausible results.

The ERG's modelling of overall survival is the most appropriate for decision making

3.15 In its base case, the ERG used the log-logistic curve for gefitinib and the fractional polynomial network meta-analysis for the other comparators (P1=0.5, P2=1). It assumed equal efficacy for overall survival between all treatments after 36 months. The ERG acknowledged that assuming equal efficacy from 48 or 60 months could also be considered plausible and explored these in scenario analyses. The ERG also did a scenario analysis in which it assumed equivalent post-progression survival for all

treatments. It agreed that there was uncertainty around the company's modelling of overall survival because of the implausibility of the results. The committee therefore agreed that the ERG's modelling of overall survival should form the basis of its decision making.

Health-related quality of life

The model should include age-related disutilities

3.16 For progression-free disease, the company used utility values from ARCHER 1050 for dacomitinib and gefitinib (the company considers the values to be academic in confidence and therefore cannot be reported here). The company assumed that the utility value for afatinib would be equivalent to that of dacomitinib, and that the value for erlotinib would be equivalent to that of gefitinib, based on the similarity of their respective adverse-event profiles. The committee considered that it was appropriate for the company to assume equivalent utility values in this way. However, the company did not include any age-related disutilities. The committee accepted that these should have been included in the model given both the starting age of the population modelled and the length of the time horizon.

Using utility values for progressed disease from ARCHER 1050 is more appropriate

3.17 For progressed disease, the company used a utility value of 0.64 from Labbe (2017). The ERG considered it more appropriate to use utility values from ARCHER 1050 for progressed disease, because there were limitations with the data from Labbe (including differences in patient baseline characteristics between ARCHER 1050 and Labbe, in particular the exclusion of people with brain metastases from ARCHER 1050). However, the clinical experts commented that the difference between these utility values (that is, from ARCHER 1050 and Labbe) would be unlikely to translate into a clinically meaningful difference. The committee acknowledged that the utility value for progressed disease was not a

significant factor in the cost-effectiveness analysis. However, from a methodical perspective, it may be more appropriate to use utility values from trials when they are available. So, the committee considered it appropriate to use utility values from ARCHER 1050 for progressed disease.

The analyses should include disutilities associated with adverse events

3.18 In its base case the company did not include any disutilities for adverse events, but incorporated a one-off treatment-specific disutility in a scenario analysis. The company's rationale for not including these disutilities was that the utility values from ARCHER 1050 would already incorporate the effect of adverse events through EQ-5D-3L data collected during the trial. To include treatment-specific utility decrements for adverse events would effectively double count the effect of adverse events on the utility values. However, the ERG considered that the base-case analysis should include treatment-specific disutilities for adverse events. Many of the most common adverse events are limited in duration, and the EQ-5D-3L only captures how people feel on the day that they complete it. The clinical experts also explained how the EQ-5D-3L does not capture the full impact of certain adverse events, such as diarrhoea, on health-related quality of life. The committee concluded that it was more appropriate to include disutilities associated with adverse events in the base-case analyses.

Resource use and costs

The company's assumptions about health benefits and costs of subsequent therapies are implausible

3.19 In its base case, the company assumed that 71% of people having tyrosine kinase inhibitors would also have disease progression and second-line treatment. Of these, 56% would develop the T790M mutation and have osimertinib and the other 44% would have chemotherapy. The model also assumed that 48% of the original cohort would have third-line

treatment; of these, 56% would have chemotherapy (the same people who had second-line osimertinib) and 44% would have docetaxel (the same people who had second-line chemotherapy). The committee was aware of NICE's statement on handling comparators and treatment sequences on the Cancer Drugs Fund, specifically that 'products recommended for use in the Cancer Drugs Fund after 1 April 2016 should not be considered as comparators, or appropriately included in a treatment sequence, in subsequent relevant appraisals'. The committee accepted that it was appropriate for osimertinib to be included in the treatment sequence in the model for dacomitinib, because this appraisal started before the position statement came into effect. The committee noted that the proportions and subsequent treatments used in the model did not reflect those used in ARCHER 1050 (see section 3.6). The clinical lead for the Cancer Drugs Fund explained that the proportions of people having second- and third-line treatments were higher than those seen in NHS clinical practice (50% to 60% for second line and 25% to 30% for third line). Also, osimertinib has been used less than would be expected in NHS clinical practice in England (8% to 13%), so the model overestimates its use. The clinical experts agreed that the proportions of people having subsequent treatments in the model were too high. The committee understood that the company had used the same proportions for second- and third-line treatments for all 4 tyrosine kinase inhibitors; so, although the exact proportions were inaccurate, the costs applied to the dacomitinib and comparator treatment arms were the same. But the committee recalled that the model did not capture the clinical benefits of subsequent treatment. It concluded that the company's assumptions about treatment costs and benefits in the model did not reflect the type and proportion of subsequent treatments received by patients in the trial.

Results of the cost-effectiveness analyses

The assumptions in the ERG's base case are more appropriate for decision making

3.20 The ERG's base-case model incorporated the committee's preferred assumptions:

- For progression-free survival:
  - using the log-normal parametric curve for gefitinib and the fractional polynomial network meta-analysis (P1=0.5, P2=1) for the other comparators
  - assuming progression-free survival with afatinib to be equal to the mean progression-free survival of dacomitinib and gefitinib after 36 months (see section 3.13).
- For overall survival:
  - using the log-logistic parametric curve for gefitinib and the results from the fractional polynomial network meta-analysis (P1=0.5, P2=1) for the other comparators
  - assuming equal efficacy for all treatments after 36 months (see section 3.15).
- Including age-related disutilities (see section 3.16).
- Using utility values for progressed disease from ARCHER 1050 (see section 3.17).
- Including disutilities associated with adverse events (see section 3.18).

The committee concluded that the ERG's base case was more appropriate than the company's for decision making. However, it noted that neither the ERG's nor the company's base case included accurate health benefits and costs of subsequent therapies.

The most plausible cost-effectiveness estimates for dacomitinib are over £30,000 per quality-adjusted life year gained

3.21 Because dacomitinib and the comparators have commercial arrangements, the exact incremental cost-effectiveness ratios (ICERs) are confidential and cannot be reported here. The committee noted that the ERG's base case produced a deterministic ICER for dacomitinib of over £30,000 per QALY gained. The committee noted that a number of the ERG's scenario analyses produced ICERs that were lower than the base-case estimate (specifically, assuming the progression-free survival of afatinib to be equal to the mean progression-free survival of dacomitinib and gefitinib after 55 months, assuming equal overall survival after 48 and 60 months, and assuming equivalent post-progression for all treatments). But the committee noted that in all these scenario analyses, the ICER for dacomitinib was still over £30,000 per QALY gained.

End of life

Dacomitinib does not meet the end-of-life criteria

3.22 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's Cancer Drugs Fund technology appraisal process and methods. The company submission stated that dacomitinib does not meet the end-of-life criteria. The committee considered the clinical evidence and agreed that life expectancy for people with untreated locally advanced or metastatic EGFR mutation-positive NSCLC having standard care is more than 2 years: in ARCHER 1050, the median overall survival with gefitinib was 26.8 months (95% CI 23.7 to 32.1). The committee therefore concluded that dacomitinib did not meet the end-of-life criteria in this indication.

Innovation

The model adequately captures the benefits of dacomitinib

3.23 The company considered dacomitinib to be innovative, highlighting that it improves survival compared with gefitinib erlotinib and afatinib. The clinical experts agreed that dacomitinib is an effective second-generation tyrosine kinase inhibitor and that people would welcome additional treatment options. However, they also highlighted that there is no evidence to support dacomitinib's use in patients with brain metastases because they were excluded from ARCHER 1050. The committee concluded that it had not been presented with any additional evidence of benefits that were not captured in the measurement of the QALYs and the resulting cost-effectiveness estimates.

Routine NHS use

Dacomitinib is not recommended for routine use in the NHS for untreated locally advanced or metastatic EGFR mutation-positive NSCLC in adults

3.24 Having considered all the available evidence for dacomitinib, the committee concluded that dacomitinib was not a cost-effective use of NHS resources for untreated locally advanced or metastatic EGFR mutation-positive NSCLC.

Cancer Drugs Fund

Dacomitinib is not recommended for use in the Cancer Drugs Fund

3.25 Having concluded that dacomitinib is not recommended for routine use, the committee then considered if it could be recommended for use within the Cancer Drugs Fund. The company did not express an interest in dacomitinib being considered for funding through the Cancer Drugs Fund. The committee recognised that the clinical data from ARCHER 1050 was relatively mature so there was little uncertainty that would be resolved through further data collection. The committee also noted that when taking

into account the commercial arrangements for dacomitinib and the comparators, all the most plausible ICERs were over £30,000 per QALY gained. Given that dacomitinib does not meet the end-of-life criteria, the committee concluded that dacomitinib does not have plausible potential to be cost effective at its current price, and so could not be recommended for use within the Cancer Drugs Fund.

Other factors

3.26 No equality or social value judgement issues were identified

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Professor Gary McVeigh
Chair, appraisal committee
April 2019

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

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.

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.

Luke Cowie
Technical Lead

Nicola Hay
Technical Adviser

Joanne Ekeledo
Project Manager

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