# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Draft guidance consultation

# Osimertinib with pemetrexed and platinum-based chemotherapy for untreated EGFR mutation-positive advanced non-small-cell lung cancer [ID6328]

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using osimertinib with pemetrexed and platinum-based chemotherapy in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

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

The evaluation 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 age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?



Issue date: October 2024

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

After consultation:

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- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using osimertinib with pemetrexed and platinum-based chemotherapy in the NHS in England.

For further details, see NICE’s manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 20 November 2024
- Second evaluation committee meeting: 15 January 2025
- Details of membership of the evaluation committee are given in section 4

# 1 Recommendations

1.1 Osimertinib with pemetrexed and platinum-based chemotherapy is not recommended, within its marketing authorisation, for untreated advanced non-small-cell lung cancer (NSCLC) in adults whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

1.2 This recommendation is not intended to affect treatment with osimertinib with pemetrexed and platinum-based chemotherapy 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 healthcare professional consider it appropriate to stop.

**Why the committee made these recommendations**

Usual treatment for untreated advanced NSCLC with EGFR mutations is osimertinib alone.

Clinical trial evidence shows that, compared with osimertinib alone, osimertinib with pemetrexed and platinum-based chemotherapy increases how long people have before their cancer gets worse and how long they live. But the effect on how long people live is uncertain because there is limited clinical trial evidence.

There are also issues with the assumptions used in the economic model. These include:

- how long people live
- how long people have the treatment
- quality of life before the cancer gets worse.

Because of the uncertainties in the economic model, it is not possible to determine the most likely cost-effectiveness estimates for osimertinib with pemetrexed and

platinum-based chemotherapy. So, it has not been shown to be a cost-effective option and it is not recommended.

# 2 Information about osimertinib with pemetrexed and platinum-based chemotherapy

## Marketing authorisation indication

2.1 Osimertinib with pemetrexed and platinum-based chemotherapy (Tagrisso, AstraZeneca) is indicated for 'the first-line treatment of adult patients with advanced NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations'.

## Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for osimertinib.

## Price

2.3 The list price of osimertinib is £5,770 per pack of 30 tablets in either 40-mg or 80-mg doses (excluding VAT; BNF online accessed October 2024).

2.4 The list price of pemetrexed (25 mg/ml) varies between £128 and £160 per 4-ml vial, between £640 and £800 per 20-ml vial, between £1,280 and £1,600 per 40-ml vial, and is £1,360 per 34-ml vial (excluding VAT; BNF online accessed October 2024).

2.5 The company has a commercial arrangement. This makes osimertinib available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. The size of the discount is commercial in confidence.

# 3 Committee discussion

The evaluation committee considered evidence submitted by AstraZeneca, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

## Clinical management

### Current management

3.1 The scope for this evaluation included several different treatment options for previously untreated epidermal growth factor receptor (EGFR)-positive non-small-cell lung cancer (NCSLC) as possible comparators, including osimertinib monotherapy. The company suggested that standard care is osimertinib monotherapy, which the clinical experts and EAG agreed with. This evaluation assesses the clinical and cost effectiveness of adding pemetrexed and platinum-based chemotherapy to osimertinib.

### Patient expert perspectives

3.2 Clinical and patient experts explained that although introducing osimertinib improved outcomes for people with previously untreated EGFR-positive NSCLC, progression is likely to happen eventually. The patient expert's statement noted that treatment options that extend life are welcomed. But they also explained that the side effects of osimertinib, which in their experience included diarrhoea, appetite loss and skin rashes, can be difficult to manage. They explained that the likelihood of additional side effects caused by adding chemotherapy to osimertinib monotherapy was concerning. The patient expert added that osimertinib is an oral tablet that can be taken at home. This is less of a physical and emotional burden than travelling to hospital, which would be required for treatment with chemotherapy. The committee concluded that people with untreated EGFR-positive NSCLC would welcome another treatment option, but the additional side effects and burden from adding chemotherapy to osimertinib monotherapy should be considered.

# Clinical effectiveness

## FLAURA2

3.3 FLAURA2 is an ongoing multicentre, open-label, randomised phase 3 clinical trial comparing osimertinib plus pemetrexed and platinum-based chemotherapy with osimertinib alone. The primary outcome of the trial was progression-free survival. Secondary outcomes included overall survival, time to treatment discontinuation (TTD) and health-related quality of life. The trial enrolled 557 people with previously untreated EGFR-positive locally advanced or metastatic NSCLC. A total of 279 people had osimertinib with pemetrexed and platinum-based chemotherapy and 278 had osimertinib alone. Progression-free survival was reported for the primary analysis point (April 2023). The results indicated that osimertinib with pemetrexed and platinum-based chemotherapy was significantly more effective at preventing progression or death than osimertinib alone (hazard ratio [HR] 0.62, 95% confidence interval [CI] 0.49 to 0.79, p<0.001). Overall survival was reported from the second interim analysis (January 2024). The results indicated that osimertinib with pemetrexed and platinum-based chemotherapy was significantly more effective at preventing death than osimertinib alone (HR 0.75, 95% CI 0.57 to 0.97). The committee concluded that osimertinib with pemetrexed and platinum-based chemotherapy was an effective treatment for previously untreated EGFR-positive locally advanced or metastatic NSCLC.

## Central nervous system metastases subgroup

3.4 FLAURA2 included several prespecified subgroups, including people with central nervous system (CNS) metastases at baseline. In its analysis of the trial results, the EAG noted that osimertinib with pemetrexed and platinum-based chemotherapy appeared to have comparatively greater effectiveness for people who had CNS metastases at baseline than those who did not. In the subgroup of people who had CNS metastases at baseline, the osimertinib with pemetrexed and platinum-based

chemotherapy arm had a progression-free survival HR of 0.47 (95% CI 0.33 to 0.66). By comparison, in people who did not have CNS metastases at baseline, the HR was 0.75 (95% CI 0.55 to 1.03). The clinical expert noted that, unless there are clinical signs, people with previously untreated EGFR-positive locally advanced or metastatic NSCLC are not typically scanned for CNS metastases. They highlighted that everyone in FLAURA2 was scanned for CNS metastases at baseline. This meant that a larger proportion of people in FLAURA2 were identified as having CNS metastases than would be expected to be identified in NHS practice. The clinical expert also noted that scanning for CNS metastases in everyone with previously untreated EGFR-positive locally advanced or metastatic NSCLC would be difficult to implement in the NHS. The NHS England clinical lead for the Cancer Drugs Fund (from here, the Cancer Drugs Fund lead) noted that there may be a risk of overdiagnosis if everyone with EGFR-positive locally advanced or metastatic NSCLC is scanned. This is because CNS metastases that are not clinically relevant and do not cause accompanying symptoms may be identified, and this could affect the everyday lives of people with EGFR-positive NSCLC. They also noted that additional scans would potentially delay treatment starting. The committee recognised that the clinical trial results indicated that people with CNS metastases at baseline may have different outcomes to those without. But it did not believe that people with CNS metastases before treatment would be identified in NHS practice without significant changes to the way this disease is managed. The committee was also unclear why the addition of chemotherapy to osimertinib produced such different results in people with CNS metastases. It also noted that the costs associated with an increase in testing for CNS metastases had not been taken into account in the analysis. The committee concluded that it would not consider people with CNS metastases at baseline separately, because:

- this population is not routinely identified in clinical practice

- there are risks associated with overdiagnosis and treatment delay if scans for CNS metastases are routinely used, and
- the company's model did not include costs associated with scans for CNS metastases.

## Generalisability

3.5 The EAG noted several issues that could affect the generalisability of the results of FLAURA2 to NHS practice. First, it noted that FLAURA2 participants were, on average, younger than the NHS population of people with EGFR-positive locally advanced or metastatic NSCLC. It also noted that the second- and third-line treatments used during the trial might not match those used in the NHS (see section 3.13). Finally, the EAG highlighted that the proportion of people in FLAURA2 with CNS metastases at baseline may have been larger than in NHS practice, which may have overestimated the average treatment effect (see section 3.4). The EAG recommended that the starting age in the model be changed from 61 (the average age in FLAURA2) to 65.6 (the average age from published UK survey data [Molife et al. 2023]). The company highlighted that it consulted a UK advisory board, which advised that the FLAURA2 patient population was representative of the UK EGFR-positive locally advanced or metastatic NSCLC population. The clinical expert noted that many people with CNS metastases would not be identified in NHS practice, so the proportion of people with CNS metastases in FLAURA2 may be closer to reality. The Cancer Drugs Fund lead advised that the mean age of people with EGFR-positive locally advanced or metastatic NSCLC in the NHS was 68.5 and the median age was around 70. But, they noted that the average age may be lower for people having osimertinib with pemetrexed and platinum-based chemotherapy because of the treatment burden of chemotherapy. The committee concluded that the FLAURA2 population was likely to be younger than the NHS population, so it preferred the EAG's approach of using a starting age of 65.6 in the model. It also concluded that, overall, FLAURA2 was

generalisable to practice in the NHS. But, it noted that the proportion of people with CNS metastases and the second- and third-line treatments used, were different in FLAURA2 and NHS practice, which contributed to uncertainty around the treatment effect.

## Economic model

### Company's modelling approach

3.6 The company used a partitioned survival model with 3 health states: progression free, progressed disease, and death. The committee considered that the partitioned survival model is a standard approach to estimate the cost effectiveness of cancer drugs and is suitable for decision making.

### Extrapolation of overall survival

3.7 The company analysed overall survival data from the second interim analysis (January 2024). It found that the data violated the proportional hazards assumption. So, it produced separate extrapolation models for each treatment arm. The EAG agreed that the data violated the proportional hazards assumption and that separate curves for each arm were appropriate. The company selected a 2-knot spline model on a normal scale for both treatments in its base case. For the osimertinib with pemetrexed and platinum-based chemotherapy arm, this was because it gave the best statistical fit of the spline models and a potentially conservative estimate of long-term survival. The company noted that the extrapolations produced by the 2-knot spline model on a normal scale for the osimertinib monotherapy arm were in line with feedback from its clinical advisers. The EAG disagreed with the company's model selection for the osimertinib monotherapy arm. It noted that all the 1-knot spline models fit the osimertinib monotherapy arm better than the 2-knot models. The EAG believed this indicated that the most suitable extrapolations for each arm would have different shapes. It considered this clinically plausible because chemotherapy has a different mechanism of action

from osimertinib. The EAG considered the FLAURA2 overall survival data, and data from a Dutch registry study (Gijtenbeek et al. 2023) to validate the extrapolations. It also considered the point when treatment in both arms would be expected to have stopped, at which point survival in each arm would be expected to converge. When considering this data, the EAG selected:

- a 1-knot spline model on the odds scale for the osimertinib monotherapy arm, and
- a 2-knot spline model on the odds scale for the osimertinib with pemetrexed and platinum-based chemotherapy arm.

The committee noted that using different numbers of knots for each arm requires significant justification. It concluded that both the EAG's and company's approach to modelling overall survival had methodological strengths and limitations and that either might be appropriate. But, it also concluded that both are associated with uncertainty, so it requested more justification for the choice of overall survival model.

## Extrapolation of TTD

3.8 The extrapolation of TTD was a major driver of the model, and substantially affected the cost-effectiveness estimates. The company modelled the TTD for the osimertinib and pemetrexed components of the osimertinib with pemetrexed and platinum-based chemotherapy arm separately. The company selected the Gompertz model for the osimertinib component and the exponential model for the pemetrexed component. TTD for the platinum-based chemotherapy component was not modelled because platinum-based chemotherapy was given for a fixed number of treatment cycles. The EAG agreed that these choices were the most suitable for that arm. For the osimertinib monotherapy arm, the company used the gamma model, which had the second-best statistical fit. The

EAG noted that almost all the TTD extrapolations produced by the company for the osimertinib monotherapy arm were significantly above the extrapolation of progression-free survival. So, the EAG considered most of the company's extrapolations of TTD to be implausible, because osimertinib treatment would not continue for a significant period of time after disease progression. It proposed using a Gompertz model for TTD extrapolation in the osimertinib monotherapy arm. In this model, people were modelled to have osimertinib for less time than in the company's model. The Gompertz model was selected because although the model fit statistics were the least good of all the curves, they were adequate and similar to the model fit statistics for all other curves; the visual fit to the observed data was good; and the extrapolation was plausible compared with the curve used for progression-free survival. The clinical expert explained that osimertinib may be used beyond progression, so progression-free survival and TTD curves do not necessarily need to be precisely aligned. The committee noted that in FLAURA2, there was longer treatment beyond progression with osimertinib monotherapy than with osimertinib with pemetrexed and platinum-based chemotherapy. The clinical expert suggested that, by the time progression has occurred, most people in both arms would likely only be on osimertinib. So, in practice, the use of osimertinib post-progression was likely to be similar in both arms. The committee considered that the observations in the trial were not explained. The committee also discussed whether the difference observed in treatment beyond progression in FLAURA2 would be reflective of the difference in treatment beyond progression in the longer term. The clinical expert noted that treatment with osimertinib would continue for less time following progression if there was early progression or primary resistance than if progression happens after several years. The clinical expert believed that the true TTD was likely to be between the company's and the EAG's extrapolations. The committee considered that there was not enough evidence to support either the company's or the EAG's base-case model selection. The committee concluded that:

- TTD was a key driver of the cost-effectiveness modelling but that it had not been presented with robust long-term estimates to use in decision making.
- It is plausible that TTD is longer than progression-free survival because osimertinib may be used following progression.
- Once pemetrexed and platinum-based chemotherapy has stopped (around 8 months in FLAURA2), the gap between progression-free survival and TTD is expected to be similar in both arms.
- The difference in TTD and progression-free survival in the trial may not be reflective of osimertinib's use following progression after several years. In the absence of other evidence, it may be appropriate to consider analysis reflecting the difference in TTD and progression-free survival in the trial, but that further explanation is needed.

The committee requested further analyses that provides plausible TTD extrapolations, particularly considering the relationship with the progression-free survival extrapolation. It requested that these include:

- a scenario in which both treatment arms are modelled to have the same time between progression and treatment discontinuation once pemetrexed and platinum-based chemotherapy have stopped
- cross-validation of TTD extrapolations with other osimertinib monotherapy TTD data, for example from FLAURA, and
- a scenario that better reflects the difference in TTD and progression-free survival in the trial in both arms and that reflects expected clinical practice.

## Utility values

### Progression-free health state utility

3.9 The company used EQ-5D-5L responses from FLAURA2, mapped to the EQ-5D-3L using the Hernández-Alava algorithm, to estimate a utility value

for the progression-free health state for both arms (the exact utility value is considered confidential by the company so cannot be reported here). It used a mixed model for repeated measures (MMRM), and explained that this accounted for missing data. The company also applied a disutility to the osimertinib with pemetrexed and platinum-based chemotherapy arm in the first model cycle to account for adverse effects due to chemotherapy. The EAG raised several concerns about the company's approach to estimating the progression-free health state utility values. First, it noted that the company's progression-free utility was higher than the average utility for the general population (0.799 for people aged 55 to 64). To explain the overestimation, the EAG noted that the MMRM was unlikely to be suitable for adjusting the FLAURA2 responses for missing data. MMRM requires data to be missing at random, and the EAG highlighted that in the osimertinib with pemetrexed and platinum-based chemotherapy arm, there was a higher proportion of missing data during the first 16 weeks of the trial, which is when people were having chemotherapy. It noted that utility values would be expected to be lower for people having chemotherapy. The EAG also suggested that the Hernández-Alava algorithm may overestimate utility in people with NSCLC. The EAG also highlighted concerns with the disutility applied to account for chemotherapy-related adverse events. It believed that the disutility applied was too small because it did not account for interactions between adverse events. It also believed that the disutility would last longer than the first model cycle. The EAG suggested an alternative approach to the progression-free health state utility value. It recommended using the progression-free utility value of 0.794 from NICE's technology appraisal on osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer. The EAG also recommended using a utility decrement applied to the entire progression-free period in the osimertinib with pemetrexed and platinum-based chemotherapy arm. This was to account for the impact of chemotherapy on quality of life. To calculate a decrement, the EAG considered the improvement in utility from baseline to the mean

progression-free period between arms. The improvement was greater in the osimertinib monotherapy arm, so the EAG believed the difference between the improvements represented the negative effect of chemotherapy on quality of life (the exact figure is considered confidential by the company so cannot be reported here). It also said that individualised utility data from the first 16 weeks of the trial would help reduce uncertainty around the duration and magnitude of disutility related to using chemotherapy. The patient expert highlighted that side effects from osimertinib were already difficult for people to manage. The clinical expert noted that adding chemotherapy would be likely to make the adverse effects of treatment worse, so quality of life would be lower when people were having chemotherapy. They also noted that adverse events from chemotherapy would continue for 1 to 2 months after treatment with chemotherapy had stopped. The committee believed that the company's progression-free utility value lacked face validity. So, it preferred the EAG's approach to estimating the progression-free health state utility value, but noted that there was still a large amount of uncertainty regarding the true value. To reduce the uncertainty, the committee requested additional analyses that accurately captures the health-related quality of life in the progression-free state. This should include the size and duration of the impact of chemotherapy on health-related quality of life in the osimertinib with pemetrexed and platinum-based chemotherapy arm. Such analyses could also include:

- further modelling of the progression-free utility value to account for missing data
- utility data from the first 16 weeks of the trial to inform the appropriate utility decrement associated with chemotherapy
- using treatment arm as a covariate to produce treatment-specific utility values.

## Progressed-disease health state utility

3.10 The company sourced the utility value for the progressed-disease health state of 0.64 from Labbé et al. (2017).This is a Canadian longitudinal cohort study of NSCLC that included 183 people whose cancer had EGFR mutations. The company noted this utility value was similar to those accepted in previous NSCLC appraisals. The EAG noted that the high utility value of the progression-free health state (see section 3.9) meant that the difference between the 2 health states was larger than is typically seen in appraisals of NSCLC. The EAG preferred to use the progressed-disease utility value of 0.678 from NICE's technology appraisal on osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer. The committee agreed with the EAG and concluded that a utility value of 0.678 for the progressed-disease health state was most suitable.

## Modelling of chemotherapy

3.11 The EAG noted some concerns with how chemotherapy was modelled. First, the company assumed that, for those having platinum-based chemotherapy, 50% of people would have cisplatin and 50% would have carboplatin. Clinical advice to the EAG suggested that carboplatin is preferred to cisplatin in NHS practice. So, in the EAG's base case, everyone having platinum-based chemotherapy had carboplatin. The EAG also noted that the company assumed that cisplatin and carboplatin would have 100% relative dose intensity (RDI), because RDI data for cisplatin and carboplatin was not captured in FLAURA2. The EAG preferred using an RDI of 96.4% for cisplatin and carboplatin, which was accepted in NICE's technology appraisal of pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer. The committee noted that the impact of these assumptions on the incremental cost-effectiveness ratio (ICER) was negligible. It concluded that the assumptions chosen around modelling of chemotherapy did not have an impact on decision making.

# Costs

## Resource use

3.12 The company used Brown et al. (2013), updated based on advice from its clinical experts, to estimate resource use in the model. It produced separate resource use numbers for the progression-free and progressed-disease health states. The company considered resource use per person per year for:

- outpatient visits
- MRI scans
- chest CT scans
- other CT scans
- ECGs
- clinical nurse contact time and
- accident and emergency visits.

Based on advice from its clinical experts, the EAG provided amended estimates of resource use. The Cancer Drugs Fund lead generally agreed with the EAG's proposed resource use. But, they believed that the company's estimation of outpatient visits was more accurate. The committee concluded that it was appropriate to model resource use based on the company's estimation of outpatient visits and the EAG's estimations for the other resources.

## Resource cost

3.13 To produce the costs for the resources used in the model, the company used a combination of the NHS payment scheme 2023 to 2025 tariffs and Personal Social Services Research Unit costs (PSSRU, 2022). The EAG believed that NHS reference costs 2021 to 2022 better represented the true opportunity cost to the NHS of the resource use in the model. The NICE technical team noted that NHS reference costs are typically used in

technology appraisals. But both represented costs relevant to the UK healthcare system so are in accordance with NICE's guide to the methods of technology appraisal. The committee concluded that the EAG's approach to using NHS reference costs better represented costs in the NHS.

## Distribution of second-line treatments

3.14 The company modelled the treatments people would have after completing treatment with the osimertinib regimens. It used data from FLAURA2 to estimate the distribution of these treatments, then validated the results with its clinical experts. The company's clinical experts noted that in NHS practice some people would have atezolizumab, bevacizumab, carboplatin and paclitaxel combination therapy (ABCP). This was not available as a subsequent treatment in the trial. But, because it is used in clinical practice, the company included a proportion of second-line ABCP use in its model (the exact figure is considered confidential by the company so cannot be reported here). The EAG believed the company's figure for ABCP use was too high, based on advice from its clinical experts. The EAG noted that this was particularly relevant because a larger proportion of people in the osimertinib monotherapy arm had second-line treatment than in the osimertinib with pemetrexed and platinum-based chemotherapy arm (the exact figures are considered confidential by the company so cannot be reported here). It also noted that the company's model included only the costs, not the benefits, of subsequent treatment. The EAG noted this is common in cost-effectiveness modelling but, because ABCP was not used in the trial, it did not capture the benefits of second-line ABCP. So, the EAG did not include second-line ABCP in its base case. The Cancer Drugs Fund lead estimated that 6% to 7% of people with EGFR-positive locally advanced or metastatic NSCLC would have second-line ABCP, which is lower than the company's estimation. The committee recognised that a proportion of people with EGFR-positive locally advanced or metastatic NSCLC would

have second-line ABCP. But, it also recognised that the benefits of this treatment were not captured in the modelling. The committee concluded that the EAG's base case was preferable because it aligned costs and outcomes. But it also requested a scenario that included 7% of people having second-line ABCP.

## Cost-effectiveness estimates

### Company and EAG cost-effectiveness estimates

3.15 The company's and the EAG's base cases differed across several key issues. The biggest driver of the difference in cost-effectiveness estimates was the choice of TTD extrapolation (see section 3.8). The company's base-case ICER was above £20,000 per quality-adjusted life year (QALY) gained. The EAG's base-case ICER was significantly above £20,000 per QALY gained. The exact figures include confidential discounts for treatments in the pathway so cannot be reported here.

### Committee's preferred assumptions

3.16 The committee considered the analysis from the company and EAG. Its preferred assumptions were as follows:

- starting age of 65.6 years in the model (see section 3.5)
- progressed-disease utility of 0.678 (see section 3.10)
- resource use figures using the company's estimation of outpatient visits and the EAG's estimations for the other resources (see section 3.12)
- resource use costs using NHS reference costs (see section 3.13)
- 0% ACBP use at second line in the model (see section 3.14).

The committee accepted the following changes the EAG made to the company's model, which had a negligible impact on the ICER:

- 100% carboplatin use for platinum-based chemotherapy (see section 3.11)

- RDI of 96.4% for cisplatin and carboplatin (see section 3.11).

The committee could not identify a plausible ICER because further analysis was needed. The committee also could not determine where the ICER would need to be within NICE's normal cost-effectiveness range to be considered cost-effective. This was because it needed to take into account further analyses to understand the level of uncertainty associated with the modelling. The committee requested further analysis of:

- extrapolation of overall survival (see section 3.7)
- extrapolation of TTD (see section 3.8)
- progression-free health state utility (see section 3.9).

The committee also requested a scenario in which second-line treatment distributions include 7% of people having ABCP (see section 3.14).

## Other factors

### Equality

3.17 The committee noted that people with an Asian family background were more likely to have EGFR-positive advanced NSCLC. Race is protected under the Equality Act 2010. But because its recommendation does not restrict access to treatment for some people over others, the committee agreed this was not an equalities issue.

### Uncaptured benefits

3.18 The committee considered whether there were any uncaptured benefits of osimertinib with pemetrexed and platinum-based chemotherapy. It did not identify any benefits that had not already been captured in the economic modelling. So, the committee concluded that all benefits of osimertinib with pemetrexed and platinum-based chemotherapy had been taken into account.

# Conclusion

## Osimertinib with pemetrexed and platinum-based chemotherapy is not recommended

3.19 The committee had concerns with the analysis of several key issues including the extrapolation of overall survival (see section 3.7), the extrapolation of TTD (see section 3.8), and the progression-free health state utility (see section 3.9). So, it was unable to establish that osimertinib with pemetrexed and platinum chemotherapy is a cost-effective use of NHS resources. The committee concluded that osimertinib with pemetrexed and platinum-based chemotherapy is not recommended, within its marketing authorisation, for untreated EGFR mutation-positive advanced NSCLC in adults, and that further analysis is needed.

## Managed access

3.20 Having concluded that osimertinib with pemetrexed and platinum-based chemotherapy could not be recommended for routine use, the committee then considered if it could be recommended with managed access for untreated EGFR-positive advanced NSCLC. The committee noted that one of the key uncertainties was extrapolation of TTD (see section 3.8). But, the company stated that further TTD data was not likely to be reported from FLAURA2. The committee believed this meant that managed access would be unlikely to resolve all the key uncertainties. The committee noted that a managed access proposal had not been provided by the company and there was not yet a plausible cost-effectiveness estimate. So, a recommendation with managed access was not an option.

# 4 Evaluation committee members and NICE project team

## Evaluation 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 being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

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

## Chair

**Megan John**

Chair, technology appraisal committee D

## NICE project team

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

**George Millington**

Technical lead

**Albany Chandler**

Technical adviser

**Leena Issa**

Project manager

**Ian Watson**

Associate director

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