NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection

1 Recommendations

1.1 Osimertinib is recommended for use within the Cancer Drugs Fund as adjuvant treatment after complete tumour resection in adults with stage 1b to 3a non-small-cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations. It is recommended only if:

- osimertinib is stopped at 3 years, or earlier if there is disease recurrence or unacceptable toxicity and
- the company provides osimertinib according to the managed access agreement.

1.2 This recommendation is not intended to affect treatment with osimertinib 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.

Issue date: November 2021

Why the committee made these recommendations

There are currently no targeted adjuvant treatments (including those specific to EGFR mutations) available in England for NSCLC after complete tumour resection.

Current clinical trial evidence shows that compared with active monitoring, treatment with osimertinib reduces the risk of the disease coming back. It may also lower the risk of death. However, this evidence is uncertain because information from the trial was released early and the data is still immature.

Because of this, the cost-effectiveness estimates for osimertinib are also uncertain. It has the potential to be cost effective, but more evidence is needed to address these uncertainties before it can be recommended for routine use.

Because more data is being collected that addresses these uncertainties, osimertinib is recommended for use in the Cancer Drugs Fund.

2 Information about osimertinib

Marketing authorisation indication

2.1 Osimertinib (Tagrisso, AstraZeneca) is indicated for adjuvant treatment after complete tumour resection in adult patients with stage 1b to 3a non-small-cell lung cancer whose tumours have epidermal growth factor receptor 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.

Price

2.3 The list price for 30 x 80 mg tablets is £5,770 (BNF online, accessed July 2021).

2.4 The company has a commercial arrangement. This makes osimertinib available to the NHS with a discount. The size of the discount is

commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

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

New treatment option

Patients and their families would welcome new effective treatments that reduce the risk of recurrence

3.1 Surgical removal of tumours is the preferred treatment for many people with early-stage NSCLC because it is potentially a cure. But despite the curative intent of complete resection, the disease recurs within about 5 years of surgery in 45% of patients with stage 1b, 62% with stage 2, and 76% with stage 3 disease. In the UK, around 13% of people with stage 1b NSCLC up to about 50% of people with stage 3a NSCLC have adjuvant chemotherapy after resection. Because it provides only a relatively small benefit in overall and disease-free survival compared with no chemotherapy over 5 years, many people decline adjuvant therapy. The patient experts explained that people with fully resected stage 1b to 3a EGFR mutation-positive NSCLC would welcome new effective adjuvant treatments that reduce the risk of recurrence. They highlighted that people with EGFR mutation-positive NSCLC tended to be younger than people with other types of NSCLC, so having a treatment option that delays or prevents recurrence or central nervous system (CNS) metastases is important. Being disease free allows people to spend more time working or with their families. Patient experts stated that osimertinib is also better tolerated than other tyrosine kinase inhibitors (TKIs). The committee concluded that patients and their families would welcome new, effective treatments that reduce the risk of recurrence.

Treatment pathway

Osimertinib is an oral treatment in a new place in the pathway

3.2 The only treatment currently available in England as adjuvant therapy for NSCLC (including for EGFR mutations) after complete resection is adjuvant chemotherapy, which provides a small benefit in overall survival. Treatment options for people with resectable EGFR mutation-positive NSCLC are therefore only those that are generally available and are non-targeted. The clinical and patient experts explained that osimertinib is well tolerated with manageable side effects. The patient experts explained that having an oral option would be welcomed because it would not require a visit to hospital. The committee acknowledged that positioning osimertinib as an adjuvant treatment may address an unmet need for people who have had a resection. It concluded that osimertinib is an oral treatment in a new place in the pathway.

Retreatment with osimertinib would be offered to some people whose disease has progressed

3.3 The company assumed that everyone who develops distant metastases within 5 years of starting adjuvant osimertinib treatment would have pemetrexed plus cisplatin followed by docetaxel. It assumed that after this 5-year timepoint, 50% of people who develop distant metastases would have retreatment with osimertinib as first-line therapy (see NICE's guidance on osimertinib for untreated EGFR mutation-positive NSCLC) followed by pemetrexed plus cisplatin, with the remaining 50% having pemetrexed plus cisplatin followed by docetaxel. The ERG explained that in its base case, it had included atezolizumab, bevacizumab, carboplatin and paclitaxel as a second-line treatment in both groups and that it had excluded retreatment with osimertinib in the adjuvant osimertinib group. The clinical experts suggested that people are likely to have chemotherapy or atezolizumab, bevacizumab, carboplatin and paclitaxel if their disease progresses during treatment with osimertinib, while osimertinib would be offered to people whose disease progresses after

adjuvant treatment with osimertinib. The Cancer Drugs Fund clinical lead agreed that if disease relapsed after treatment with osimertinib stopped, then retreatment would be commissioned in the NHS. They explained that this would depend on the time since finishing osimertinib and the onset of metastatic disease. If this time gap was short then there may not be much benefit, but they noted that the time gap would not need to be as long as that assumed by the company (at least 2 years, depending on when adjuvant osimertinib is taken). The Cancer Drugs Fund clinical lead also said that atezolizumab, bevacizumab, carboplatin and paclitaxel would be offered first line if treatment with tyrosine kinase inhibitors is inappropriate. The committee was concerned that the 50% split used in the company model is arbitrary. After consultation, the company provided additional sensitivity analyses where the proportion of people who had retreatment with osimertinib was varied between 40% to 60%. The committee noted that although the proportion of people having retreatment with osimertinib remained uncertain, it made no significant difference to the cost-effectiveness estimates since the cure timepoint used in the company's model coincided with when retreatment is allowed. The committee concluded that retreatment with osimertinib would be offered to some people whose disease had progressed after having osimertinib as an adjuvant treatment.

Clinical evidence

The clinical evidence for osimertinib is from ADAURA, a phase 3, randomised, placebo-controlled trial

3.4 The clinical-effectiveness evidence for osimertinib is based on the ADAURA randomised controlled trial. This is a phase 3 randomised, double-blind, placebo-controlled, multicentre trial in adults with completely resected stage 1b to 3a NSCLC (stratified by tumour stage, race (Asian versus non-Asian) and EGFR (exon 19 deletions or L858R) status). ADAURA compared adjuvant osimertinib 80 mg (n=339) with placebo (n=343) over a follow-up period of 12 and 24 weeks. Some people in both

arms of the trial also had adjuvant chemotherapy. The planned treatment duration was 3 years. However, the trial results were released 2 years early after determination of overwhelming efficacy with osimertinib. In the overall trial population, treatment with osimertinib resulted in significantly longer disease-free survival, with a lower risk of disease recurrence (hazard ratio: 0.20; 99.12% confidence intervals: 0.14, 0.30; p<0.001). However, the disease-free survival data is immature and there have been very few events from which to calculate overall survival.

It is not certain to what extent a benefit in disease-free survival translates into a benefit in overall survival

3.5 Because results of the ADAURA trial have been released 2 years early, overall survival data is immature. The company explained that even though overall survival data from ADAURA is very immature, adjuvant osimertinib is expected to have a long-term survival benefit. This is because of the size of the disease-free survival benefit, a significant reduction in central nervous system metastases, and a consistent overall survival benefit when it is used to treat metastatic disease. Both the ERG and clinical experts agreed that disease-free survival is a clinically relevant end point. The clinical experts also emphasised the important benefits of a reduction in central nervous system metastases. However, the ERG explained that because of the immaturity of the overall survival data from ADAURA, the size of any potential overall survival benefit is uncertain. The committee acknowledged that uncertainty remains around the extent to which adjuvant osimertinib prevents disease recurrence compared with delaying disease recurrence. Very few patients had reached 3 years of treatment with osimertinib and data on recurrence after stopping treatment were not presented. Therefore, it is uncertain what will happen after stopping treatment. The committee was also aware of recent publications by Gyawali (2021) and Uprety (2021), which noted that other adjuvant tyrosine kinase inhibitors showed disease-free survival benefits that have not translated to an overall survival benefit. The committee was concerned that the experience with earlier generation TKIs such as

erlotinib suggested that disease often recurred after stopping treatment. However, a clinical expert cautioned against placing too much weight on this because erlotinib does not have the same brain penetration as osimertinib. In response to consultation, the company stated that the comparison to earlier TKI data in the adjuvant setting was not appropriate. It noted that the benefits of osimertinib, particularly around reducing CNS metastases, were greater than with the earlier TKIs. However, the committee noted there is currently no evidence to show that after stopping treatment with osimertinib the hazards, and therefore the hazard ratios, for disease-free survival does not increase (as with the other TKIs). Therefore, the committee reiterated its concern over the immaturity of the disease-free survival and overall survival data as well as the uncertainty around the extent to which disease-free survival can accurately predict overall survival. The committee concluded that it was not certain to what extent a benefit in disease-free survival translates into a benefit in overall survival.

The company's economic model

The company's model structure is acceptable for decision making, but more formal statistical modelling of cure may address some uncertainty

3.6 The company used a state transition, semi-Markov model with 5 health states: disease free, loco-regional recurrence, first-line treatment for distant metastases, second-line treatment for distant metastases, and dead. In the company's model, retreatment with osimertinib for distant metastases is assumed for 50% of people, with the remaining 50% having pemetrexed plus cisplatin. The committee recalled that chemotherapy or atezolizumab, bevacizumab, carboplatin and paclitaxel would be offered to people whose disease had progressed during treatment with osimertinib. Retreatment with osimertinib would be offered to people whose disease had progressed after adjuvant treatment with osimertinib (see section 3.3). In its model, the company had also assumed that 100% of people in the active monitoring arm have osimertinib as their first

treatment for metastatic disease (see section 3.10). The ERG explained that the company's model therefore did not reflect the expected treatment pathway. After consultation, the company did additional scenario analyses:

- including proportions of 80% and 90% to represent people in the active monitoring arm having osimertinib as their first treatment for metastatic disease
- varying the proportion of people who have retreatment with osimertinib (40%, 50% and 60%).

The committee noted that these additional scenario analyses done by the company may address some concerns around the company's economic model not reflecting the treatment pathway. The company's model also included a structural cure assumption (see section 3.8). The ERG noted that the cure timepoint used in the company's model coincided with when retreatment is allowed, the latter meant that this has little impact on the ICER. The proportion of people relapsing in the model is also uncertain. The company explained that this proportion varied between its clinical experts. The ERG noted that it would have preferred to have seen formal statistical modelling of cure (for example, using a mixture-cure model). The company stated that it had attempted to fit the trial data to a mixture-cure model, but the data was too immature and gave highly uncertain results. The committee concluded that the company's model structure is acceptable for decision making, but more formal statistical modelling of cure may address some uncertainty.

Including a 3-year stopping rule is acceptable but the effect of stopping treatment at 3 years is uncertain

3.7 The company included a 3-year treatment stopping rule in its model. This is based on the trial design of ADAURA, where the maximum possible treatment duration was 3 years. It is also stated in the summary of product characteristics that treatment for more than 3 years was not studied. The

clinical experts said that adjuvant treatment could not be indefinite and that the 3-year time period is appropriate. However, the patient experts said they would prefer to continue treatment beyond 3 years if the disease had not progressed. They explained that some people would find stopping treatment difficult because they would fear the disease coming back. The committee noted that in ADAURA, 12% of patients in the intervention arm and 10% in the active monitoring arm had reached 3 years of treatment. The committee concluded that a 3-year treatment stopping rule, in line with the clinical and cost-effectiveness evidence, was acceptable but the impact of stopping treatment at 3 years is uncertain.

Modelling survival and cure assumptions

Other approaches to modelling overall survival may be plausible

3.8 The predicted overall survival gain is a function of all transitions included in the model (see section 3.6), most of which are informed by external data and the company's structural cure assumption (a reduction in risk by 95% for people without disease recurrence at 5 years in both arms). The company's choice of survival models was based on a visual inspection of the combined disease-free survival and overall survival curves, with input from its clinical experts. In line with advice in the NICE Decision Support Unit Technical Support Document 14, the company applied the same parametric curves across both treatment arms. For the transition from disease free to loco-regional recurrence, the company applied log-normal curves, whereas generalised gamma curves were applied for the transition from disease free to distant metastatic NSCLC. The committee was aware that disease-free survival was a key driver of the company's economic model. It was concerned that most of the disease-free and overall survival benefits were gained during the extrapolated period, so the choice of extrapolation has a significant effect on the results. For the transition from disease free to distant metastases, the generalised gamma chosen by the company had the best statistical fit for the placebo arm. However, the log-normal had the best fit for the osimertinib arm. The ERG

explained that because of the cure assumption, the choice of extrapolation has little effect beyond the cure timepoint. So in this situation it is appropriate to give more weight to the statistical fit to the observed data. The ERG did additional sensitivity analyses in which it applied alternative parametric survival models to represent the transition from disease free to distant metastatic NSCLC. These used a log-normal distribution in:

- both arms of the model
- the treatment arm of the model only.

In response to consultation, the company suggested that these analyses were inappropriate, because the curves cross. However, the ERG explained that this was not the case for disease-free survival overall, when the cure assumption is factored in. The committee considered that the log-normal distribution was as plausible as the generalised gamma. Usually it is appropriate to use the same distribution for both arms. However, given the cure assumption and stopping of treatment with osimertinib, the committee considered that it was possible that there might be a different profile of hazards between the 2 arms. The committee concluded that other approaches to modelling overall survival may be plausible and it would consider these in its decision making.

There is uncertainty about the company's cure assumptions

3.9 The company originally applied a 5-year cure timepoint in its modelling based on information from its clinical experts. Clinical expert advice to the ERG was that, for the active monitoring arm of the model, a 5-year cure timepoint may be appropriate, but a potential cure timepoint for the intervention arm is uncertain. The ERG did exploratory analyses to assess the effect of changing the timepoint at which the cure assumption is applied in the company's economic model. The ERG's optimistic analysis retained the company's original approach, whereas the pessimistic

analysis applied a later timepoint for cure in the adjuvant osimertinib group of 8 years (5-year cure timepoint in the active monitoring group plus the 3-year osimertinib treatment period). In response to technical engagement, the company proposed a 6-year cure timepoint, which was supported by its clinical experts. The committee was aware that the maximum follow-up period in ADAURA was 4 years, so the company's cure assumption was uncertain. Very few patients had reached 3 years of treatment with osimertinib so it is also uncertain what will happen after stopping treatment. The committee was concerned that osimertinib may only delay rather than prevent recurrence. Taking into account that there was no data on people who have stopped osimertinib treatment, and the evidence from other tyrosine kinase inhibitors used as adjuvant treatment (see section 3.5), the committee noted that the ERG's pessimistic analysis may also be plausible. After consultation, the company did a scenario analysis where the cure assumption was removed. The ERG explained that this analysis may not be meaningful because it applies parametric survival models, which do not explicitly allow for the potential of cure, to a population in whom cure is expected for a proportion of people. The committee concluded that there was significant uncertainty about the company's cure assumptions, and it would consider both of the ERG's approaches in its decision making.

It is not appropriate to assume 100% of people in the active monitoring arm have osimertinib as their first treatment for metastatic disease

3.10 NICE recently recommended osimertinib for untreated EGFR mutation-positive NSCLC for metastatic disease. The company base case assumes that 100% of people in the active monitoring arm will have osimertinib as their first treatment for metastatic disease. The committee recognised that people in the ADAURA trial are being actively monitored and disease may be identified at an earlier stage of progression than in current practice. Therefore, more people could be fit enough to have treatment, so outcomes in advanced disease could be better than seen in the FLAURA trial data. The ERG presented a scenario analysis using a different mix of

tyrosine kinase inhibitors. This was based on the latest tyrosine kinase inhibitor prescribing data as presented by the company. The committee considered that the proportion of people having osimertinib is likely to increase over time but may not reach 100%. After consultation, the company provided additional sensitivity analyses where 80% to 90% of people in the active monitoring arm had osimertinib as their first treatment for metastatic disease. It noted that the latest prescribing data shows this figure to be around 80%. The committee concluded that it was appropriate to base its decision making on the latest available prescribing data and that 80% was therefore appropriate to use in the analyses.

Health-related quality of life

The company's utility values are acceptable for decision making

3.11 The company included utility values based on EQ-5D-3L estimates from ADAURA, EQ-5D-3L estimates from FLAURA (a randomised double-blind, phase 3 controlled trial comparing osimertinib with erlotinib or gefitinib for the first-line treatment of EGFR mutation-positive advanced NSCLC), and published EQ-5D-3L estimates from the literature (Labbé et al. 2017). Disutilities associated with adverse events were based on published literature (Nafees et al. 2008, standard gamble) and on a previous appraisal of osimertinib used second line for metastatic disease (see NICE's guidance on osimertinib for EGFR T790M mutation-positive advanced NSCLC). The ERG was concerned that the utility values applied in the disease free, loco-regional recurrence and distant metastatic NSCLC health states may be implausibly high compared with the general population. The ERG was also concerned that the model does not include health-related quality of life decrements for late effects of adjuvant treatment or downstream adverse events. However, it suggested that although the utility values may have been overestimated, they did not necessarily favour osimertinib. The ERG explained that it did an additional sensitivity analysis using utility values from a study by Andreas et al. (2018). This had a limited effect on the cost-effectiveness estimates. The

committee concluded that the company's utility values were acceptable for decision making.

Cost-effectiveness estimate

The most plausible incremental cost-effectiveness ratios (ICERs) for osimertinib are highly uncertain

3.12 Because of confidential discounts for subsequent therapies, the cost-effectiveness results are commercial in confidence and cannot be reported here. However, the company's base case including all discounts was less than £20,000 per quality-adjusted life year (QALY) gained. The ERG made several changes to the company's base case and presented 2 analyses. The first was based on a 5-year cure point in both arms and produced a similar ICER to the company's base case. The second was based on an 8-year cure point in the osimertinib arm and produced an ICER greater than £20,000 per QALY gained. At the second committee meeting, the committee considered several modelling assumptions plausible:

- The ERG's optimistic base case, which included a cure point at 5 years for the osimertinib group and 5 years for the active monitoring group.
- The ERG's pessimistic base case, which included a cure point at 8 years for the osimertinib group and 5 years for the active monitoring group.
- Assuming 80% of people in the active monitoring arm have osimertinib as their first treatment for metastatic disease.
- Alternative plausible modelling assumptions for the transition from the disease free to distant metastatic NSCLC health states using a log-normal distribution in
  - both arms of the model
  - in the treatment arm of the model only.

- Including retreatment with osimertinib after recurrence in the intervention arm of the model (using proportions of 40%, 50% and 60%).

Combining any of these assumptions with the ERG's optimistic base case resulted in ICERs of below £20,000 per QALY gained. However, combining them with the ERG's pessimistic base case resulted in ICERs above £30,000 per QALY gained. Combining the ERG's pessimistic base case, 80% osimertinib treatment for first-line distant metastases and the log-normal extrapolation for the transition from the disease free to distant metastases in the treatment arm only increased the ICER substantially above £30,000 per QALY gained. Using these preferred assumptions, the committee considered that the most plausible ICERs for osimertinib were in the range of less than £20,000 per QALY gained to more than £30,000 per QALY gained.

The committee concluded that the upper end of the most plausible ICER range may not be within the range usually considered a cost-effective use of resources.

Osimertinib is not recommended for routine use in the NHS

3.13 Because results from ADAURA were released 2 years early, the disease-free survival and overall survival data for osimertinib is immature. After considering the uncertainty with the clinical evidence along with its preferred assumptions, the committee considered that the upper end of the most plausible ICER range may not be within the range usually considered a cost-effective use of resources. The committee concluded it could not recommend osimertinib for the adjuvant treatment of stage 1b to 3a NSCLC after complete resection in adults whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations for routine use in the NHS.

Osimertinib is recommended for use in the Cancer Drugs Fund

3.14 Having concluded that osimertinib could not be recommended for routine use, the committee then considered if it could be recommended for treating stage 1b to 3a NSCLC within the Cancer Drugs Fund. The committee discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting NICE's Cancer Drugs Fund methods guide (addendum). The committee acknowledged that the disease-free survival and overall survival data from ADAURA was not mature and that further data collection may help address uncertainty. After consultation, the company stated that it would welcome a recommendation in the Cancer Drugs Fund if the committee recognised plausible uncertainties that would result in ICERs higher than what NICE normally considers a cost-effective use of NHS resources. The committee was aware that, although a period of time in the Cancer Drugs Fund may not produce enough mature overall survival data for a robust mixture-cure model, there would still be benefits:

- the disease-free survival data will be more mature
- there will be a better understanding of the impact of the 3-year stopping rule
- more data will be available to estimate the extent of the cure proportion.

The committee acknowledged that osimertinib has plausible potential to be cost effective. It understood that there is uncertainty around the cure time point, if osimertinib will prevent or only delay disease recurrence, the proportion of patients that would have retreatment with osimertinib, if the benefit in disease-free survival will translate into a benefit in overall survival and if the log-normal or generalised gamma distribution should be used to extrapolate the transition from disease free to distant metastases. If the cure time point was earlier than 8 years, then osimertinib may represent a cost-effective use of NHS resources, depending on the trajectory of disease-free survival. The Cancer Drugs

Fund clinical lead indicated that they would welcome collecting data on osimertinib through the Cancer Drugs Fund. The committee concluded that osimertinib could be recommended for use in the Cancer Drugs Fund. It noted that when the guidance is reviewed, the company should consider using formal statistical modelling of cure (for example a mixture-cure model) if the data allows (see section 3.6).

Innovation

Osimertinib is recognised as an innovative therapy in the adjuvant setting

3.15 The company said that osimertinib is innovative because there has been little innovation in adjuvant treatment for stage 1b to 3a EGFR mutation-positive NSCLC, aside from adjuvant chemotherapy, in 20 years. Osimertinib has been reviewed as part of Project Orbis because it is considered an innovative adjuvant treatment. In response to consultation, the company stated that not all additional benefits associated with osimertinib had been captured in the economic analysis. In particular, the company highlighted the effect osimertinib has on reducing CNS metastases. It stated that a utility decrement had not been applied in the modelling for people whose quality of life had declined because of CNS metastases. It therefore suggested that the ICERs were a conservative estimate. The ERG stated that it did not accept that any relevant aspects of the value of adjuvant osimertinib had clearly been omitted from the company's economic analyses. The committee recognised osimertinib as an innovative therapy in the adjuvant setting but concluded that it did not consider there were any additional benefits associated with osimertinib that had not been captured in the economic analysis.

Equality

EGFR mutation-positive NSCLC is more common in women and people with a Chinese family background

3.16 The clinical experts explained that EGFR mutation-positive NSCLC tends to be more common in women and people with a Chinese family background. The committee noted that the issue of different disease prevalence cannot be addressed in a technology appraisal.

Other factors

Less common EGFR mutations were not considered

3.17 The only EGFR mutations considered within the scope of this appraisal are EGFR exon 19 deletions or exon 21 (L858R) substitution mutations. This is in line with osimertinib's current marketing authorisation. The Cancer Drugs Fund clinical lead explained that if NICE recommends osimertinib for these mutations, NHS England would consider commissioning adjuvant osimertinib treatment for other less common EGFR mutations. The committee noted that NICE can only appraise a medicine within its marketing authorisation and welcomed the comments from the Cancer Drugs Fund clinical lead.

The end of life criteria are not met

3.18 The company did not make a case for osimertinib meeting NICE's end of life criteria. NICE's advice about life-extending treatments for people with a short life expectancy did not apply.

Conclusion

3.19 The committee recognises that osimertinib is a promising new treatment option. However, there is not enough clinical- and cost-effectiveness evidence to recommend it for routine use in the NHS. Therefore osimertinib is recommended for use in the Cancer Drugs Fund as an adjuvant treatment of stage 1b to 3a NSCLC after complete tumour

resection, in adults whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations. The committee recognised that the ADAURA trial used The Union for International Cancer Control (UICC) TNM 7th edition lung cancer staging criteria and that this evidence underpinned the marketing authorisation. It was aware that these criteria had been recently updated and that the 8th edition is also now used in NHS clinical practice. It understood from the Cancer Drug Fund clinical lead that the population as per 7th edition (stages 1b to 3a – as specified in the marketing authorisation) corresponds to stages 1b to N2 only stage 3b in the 8th edition. It also understood that the Cancer Drug Fund would ensure patient access in accordance with this translation from the 7th to the 8th edition lung cancer staging criteria.

4 Implementation

4.1 When NICE recommends a treatment as an option for use within the Cancer Drugs Fund, NHS England will make it available according to the conditions in the managed access agreement. This means that, if a patient has fully resected, stage 1b to 3a EGFR mutation-positive NSCLC and the doctor responsible for their care thinks that osimertinib is the right treatment, it should be available for use, in line with NICE's recommendations and the Cancer Drugs Fund criteria in the managed access agreement. Further information can be found in NHS England's Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for use in the Cancer Drugs Fund, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Drugs that are recommended for use in the Cancer Drugs Fund will be funded in line with the terms of their managed access

agreement, after the period of interim funding. The NHS England and NHS Improvement Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance when the drug or treatment, or other technology, is approved for use within the Cancer Drugs Fund. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, for use within the Cancer Drugs Fund, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document or agreement of a managed access agreement by the NHS in Wales, whichever is the later.

5 Review of guidance

5.1 The guidance on this technology will be considered for review 3 years after publication of the guidance. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

5.2 The data collection period is expected to end as outlined in the data collection arrangement, when the final analysis of the ADAURA study is available. Once enough evidence is available, the process for exiting the Cancer Drugs Fund will begin at this point and the review of the NICE guidance will start.

5.3 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the data collection period has ended and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of

guidance follows the standard timelines described in NICE's guide to the processes of technology appraisal.

Lindsay Smith
Chair, appraisal committee
November, 2021

6 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.

Laura Coote and Samuel Harper
Technical leads

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