NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Amivantamab for treating EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer after platinum-based chemotherapy

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using amivantamab in the NHS in England. The appraisal committee has considered the evidence submitted by the company 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, sex, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: August 2022

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 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 amivantamab 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: 16 September 2022

Second appraisal committee meeting: 5 October 2022

Details of membership of the appraisal committee are given in section 4.

1 Recommendations

1.1 Amivantamab is not recommended, within its marketing authorisation, for treating locally advanced or metastatic non-small-cell lung cancer (NSCLC) after platinum-based chemotherapy in adults whose tumours have epidermal growth factor receptor (EGFR) exon 20 insertion mutations.

1.2 This recommendation is not intended to affect treatment with amivantamab 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

Current treatment for locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations after platinum-based chemotherapy can include platinum-based chemotherapy again, immunotherapies, and docetaxel with or without nintedanib.

Indirect comparisons using real-world evidence on immunotherapies, platinum-based chemotherapy, and docetaxel with or without nintedanib, suggest that amivantamab increases how long people live, and how long they have before their cancer gets worse. But this is uncertain because there is no direct comparison, and because of the way the real-world evidence was chosen and presented. So, the cost-effectiveness estimates are also uncertain.

Amivantamab meets NICE's criteria to be considered a life-extending treatment at the end of life. But, even taking this into account, all the cost-effectiveness estimates are higher than what NICE usually considers an acceptable use of NHS resources. So, amivantamab is not recommended for routine use. Collecting more data would not resolve the uncertainties, so it is not recommended for use in the Cancer Drugs Fund.

2 Information about amivantamab

Marketing authorisation indication

2.1 Amivantamab (Rybrevant, Janssen) is indicated for the 'treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) Exon 20 insertion mutations, whose disease has progressed on or after platinum-based chemotherapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price for amivantamab is £1,079 per 50 mg vial (excluding VAT; BNF online accessed August 2022).

2.4 The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee considered evidence submitted by Janssen, 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.

Clinical management

People with EGFR exon 20 insertion mutation-positive advanced NSCLC will welcome a new treatment option that is targeted and well tolerated

3.1 The clinical experts explained that epidermal growth factor receptor (EGFR) exon 20 insertion mutations are rare and only seen in a few

people with non-small-cell lung cancer (NSCLC). Compared with other EGFR mutations, they are more commonly seen in women, people from an East Asian family background and people who do not smoke. Exon 20 insertion mutations are also associated with poorer outcomes than other EGFR mutations. The patient experts explained that, in people with exon 20 insertion mutation-positive NSCLC, the condition has a significant effect on their quality of life, and that of their families and carers. The patient experts highlighted the need for targeted treatments that have a lower toxicity and improved survival outcomes than current treatments. The clinical experts explained that there is no standard treatment for people with exon 20 insertion mutation-positive NSCLC (see section 3.2) and no treatment options that specifically target the mutations. The committee concluded that there is an unmet need for more effective treatment options that specifically target the exon 20 insertion mutations.

Comparators

EGFR tyrosine kinase inhibitors are not appropriate comparators

3.2 The clinical experts explained that there is no standard treatment pathway for people with exon 20 insertion mutation-positive NSCLC. Treatment choice depends on stage of disease, PD-L1 status, and patient and clinician preference. Treatment options can include docetaxel with or without nintedanib, immunotherapy (such as atezolizumab, nivolumab or pembrolizumab) or best supportive care. Because there is no established standard treatment pathway, the company included a blended comparator arm in its submission. This included immunotherapy treatments, EGFR tyrosine kinase inhibitors (TKIs), platinum-based chemotherapy and non-platinum based chemotherapy. The company explained that their choice of blended comparators reflected the treatments used in 2 real-world evidence sources:

- a US cohort that included pooled data from Flatiron Health Spotlight, ConcertAI and COTA data sources

- routinely collected population-level data from the National Cancer Registration and Analysis Service (NCRAS) in England.

The clinical experts explained that EGFR TKIs have limited efficacy in people with exon 20 insertion mutations. Because of this, they are rarely used and are unlikely to represent standard care in the NHS. The ERG noted that including an ineffective treatment option (that is, EGFR TKIs) in the blended comparator arm may have led to overestimating the comparative efficacy of amivantamab. However, scenario analyses excluding EGFR TKIs from the blended comparator arm had limited impact on overall survival, progression-free survival and time to next treatment estimates. The committee noted that although use of EGFR TKIs was shown in the NCRAS data, this was from a very small population and so may not reflect the broader NHS population (the population size is considered confidential by the company and cannot be reported here). The NHS England Cancer Drugs Fund clinical lead (from here, Cancer Drugs Fund lead) stated that use of EGFR TKIs use is not considered routine practice in the NHS. Considering the limitations of the available real-world evidence from England and the input from the clinical experts, the committee concluded that EGFR TKIs were not an appropriate comparator.

Using a blended comparator arm increases uncertainty

3.3 The company's approach compared amivantamab with a group of blended comparators (see section 3.2). The company explained that there was no robust way to define standard care, so it was not feasible to identify a single treatment that would be displaced by amivantamab. In addition, a fully incremental analysis is not possible when the most relevant comparator can only be accurately reflected by a blended comparator group. The committee noted that the company's approach meant that amivantamab was compared with the average clinical effectiveness across all treatments in the blended comparator group. The committee concluded that this substantially increased the uncertainty of the comparator arm evidence.

Clinical evidence

Amivantamab is clinically effective, but the size of this benefit compared with current treatments is difficult to establish

3.4 The main evidence for amivantamab came from CHRYSALIS, a single-arm, open-label, phase 1b trial. Results from March 2021 showed a median progression-free survival of 6.74 months (95% confidence interval [CI] 5.45 to 9.66) and a median overall survival of 22.77 months (95% CI 17.48 to not estimated). Overall survival results from March 2022 were also available but are considered confidential by the company and cannot be reported here. The clinical experts considered these results to be clinically meaningful. The ERG highlighted that a smaller population (n=114) was used for the CHRYSALIS efficacy analyses than for the safety population (n=153) analyses. It noted that the reason for this difference was unclear, and may have exaggerated the treatment benefits of amivantamab. During technical engagement, the company explained that a larger safety population was used to gather safety data from as large a group as possible. The company also submitted safety analyses for the smaller (n=114) population to demonstrate that similar adverse events were reported in both populations. The company did not provide updated efficacy analyses from the larger (n=153) population, and did not provide a reason for this. Overall, the committee concluded that the CHRYSALIS trial showed clinically meaningful results for amivantamab. But it thought that the lack of directive comparative evidence meant the size of this benefit compared with current treatments was difficult to establish.

The approach to using real-world evidence for the blended comparator arm may not be robust and is associated with uncertainty

3.5 There was no comparator in the CHRYSALIS trial (section 3.4) and no relevant trials were identified in a systematic literature review comparing amivantamab with the relevant comparators. So, the company did an

adjusted treatment comparison comparing amivantamab with a blended comparator (see section 3.2) using real-world evidence sources. Because exon 20 mutations affect the outcomes of people with NSCLC, the real-world evidence included was limited to people with NSCLC with these mutations. Two sources were identified: pooled US real-world evidence (used in the company base case) and evidence from the NCRAS in England (used in scenario analyses). The company explained that the US real-world evidence was chosen for the base case because of its substantially larger sample size and because clinical experts considered the evidence to be generalisable to clinical practice in England (sample sizes are considered confidential by the company and so cannot be reported here). In addition, the US real-world evidence included data on progression-free survival, time to next treatment, overall survival, and overall response rate outcomes. In contrast, the NCRAS evidence only provided data on time to next treatment and overall response rate. The ERG agreed that because of the larger sample size and because it included data on more outcomes, it was appropriate to use the US real-world evidence in the base case. However, the ERG noted that the company did not provide a full, justified rationale for its choice of real-world evidence sources and was concerned that the literature had not been reviewed systematically. So, the company may have missed relevant sources. The committee concluded that of the 2 data sources included, the pooled US real-world evidence may be the best source of evidence, but that providing outcomes for the 3 US real-world evidence sources individually and explaining why it was suitable to pool the evidence, would have reduced uncertainty. The committee noted that there may be additional relevant real-world evidence sources that were not identified by the company. It concluded that the choice of real-world evidence may not have been robust and was associated with uncertainty.

The way the company has used real-world evidence is associated with several areas of uncertainty and likely biases the results

3.6 The committee noted that, in general, there are several key differences between real-world evidence and clinical trials. Specific to this appraisal, efficacy and safety endpoints were followed up regularly in the CHRYSALIS study, but there were no scheduled visits in routine care in the real-world evidence. Also, treatment monitoring and follow up on treatment adherence may have differed between CHRYSALIS and routine care. This would have affected the efficacy and safety results. Progressed disease is less accurately captured in retrospective studies (such as from the US real-world evidence) than in prospective studies in which people generally have closer monitoring. The committee considered that despite these known limitations with real-world evidence, it can be valuable for resolving gaps in knowledge when best-practice methods are applied, such as those described in the NICE real-world evidence framework. It also acknowledged that, because of the rarity of exon 20 insertion mutation-positive NSCLC, real-world evidence may be the best available source of evidence for the comparator arm. However, the committee considered that the company had not provided enough information on data provenance, data accuracy and data suitability, and had not explored the effect of missing data. The committee concluded that the way the company had chosen and used real-world evidence was associated with several areas of uncertainty. It thought that this had likely biased the results in the modelling.

The level of uncertainty from the real-world evidence can be reduced

3.7 The committee noted that the company could have used well-validated real-world evidence checklists and reporting tools (such as the RECORD-PE checklist or the STaRT-RWE template). The company could have done a sensitivity analysis using a multiple imputation approach to assess the impact of missing data. It could also have reduced uncertainty by providing further detail on how it chose data sources and assessed their

suitability. In particular, for each of the 3 US real-world evidence sources in the company base case, further information to reduce uncertainty could have included:

- a description of each data source and the number of people included
- a description of the provenance of the data source
- further information on key study variables and outcomes, including details on data availability and completeness, how they were measured and derived from the data, whether any linkage to external data sources was included and an assessment of accuracy
- a description of the missing data and the number of people excluded from the analyses at each step of filtering (for example, how many people were filtered because of each eligibility criterion or because of missing data on key confounding variables)
- the time period when the information was collected for each variable in the real-world evidence, defined in relation to the treatment start date.

The committee also noted that a full study protocol for each of the real-world evidence sources according to the NICE real-world evidence framework requirements should be provided. The committee concluded that the level of uncertainty could be reduced if further information was to be provided, although some bias would likely remain.

Indirect treatment comparison

The company's indirect treatment comparison is suitable for decision making but is associated with uncertainty

3.8 To account for differences in patient populations between the CHRYSALIS trial and the real-world evidence sources, the company adjusted for key prognostic variables and baseline characteristics, which were identified before the analysis by a systematic literature review and validated by clinical experts. For the US real-world evidence, data was adjusted using inverse probability weighting (IPW). The company

explained that IPW was not suitable for the NCRAS evidence because of its small sample size, so it used covariate adjustment instead. Because of data availability, 8 covariates could be adjusted for in the US real-world evidence, and 7 could be adjusted for in the NCRAS evidence. The covariates adjusted for are considered confidential by the company and so cannot be described here. The ERG explained that the company's methods of adjustment appeared robust, but were limited by the covariates chosen for adjustment. Because of this, residual confounding may remain. And although using IPW appeared acceptable, alternative forms of adjustment such as propensity score matching could also be applied to the US real-world evidence. The ERG noted that propensity score matching did not improve the balance between covariates compared with the IPW method. The committee concluded that the indirect comparison using IPW for adjustment was suitable for decision making. However, it also noted that the indirect treatment comparison was associated with uncertainty. This was because of the potential residual confounding noted by the ERG and the potential evidence issues associated with the blended comparator data (see section 3.5).

Results from the indirect treatment comparison show statistically significant improvements with amivantamab, but are uncertain

3.9 The indirect comparisons showed statistically significant improvements in overall survival and progression-free survival with amivantamab compared with the blended comparator arm when the US real-world evidence was used. The committee noted that scenario analyses using the NCRAS evidence for the comparator arm increased the treatment effect of amivantamab. The exact results of the indirect treatment comparisons are considered confidential by the company and so cannot be reported here. The ERG explained that the results of the analyses were associated with uncertainties, such as being limited by the number of covariates included for adjustment (see section 3.8). Overall, the committee concluded that the indirect treatment comparison showed statistically significant

improvements with amivantamab compared with standard care, but that the exact level of improvement was uncertain.

Utility values in the economic model

It is appropriate to use utility values from past appraisals

3.10 In the base case, the company took utility values for the progression-free survival state (0.713) and post-progression state (0.569) from NICE's technology appraisal guidance on nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy (TA713). The company explained that although it had some data on quality of life from the CHRSYALIS trial, it did not use this in the model because the number of EQ-5D-5L responses from CHRYSALIS was low at time of data cut-off. It also explained that the clinical experts it consulted considered the population in TA713 appropriate to use in place of the amivantamab population. The company explained that EQ-5D-5L data from the CHRYSALIS trial was collected for only a limited number of people, and only for the progression-free survival state. The committee noted that there may have been differences between the CHRYSALIS population and the population in TA713. But it concluded that, because of the limitations of the available EQ-5D-5L data, the company's base case approach to utilities was appropriate.

Assumptions in the economic model

The company's model structure is suitable for decision making

3.11 The company used a partitioned survival model with 3 mutually exclusive health states: progression-free survival, progressed disease and death. This approach allowed the company to use outcome data from the adjusted treatment comparison. It also enabled the clinical benefits of amivantamab to be captured by reflecting the increased proportion of people expected to be alive or progression free over time. The committee agreed that the model structure was suitable for decision making.

It is appropriate to use parametric modelling for survival in the blended comparator arm

3.12 The company used Kaplan–Meier curves directly to represent survival outcomes for the blended comparator arm, and argued that this was appropriate because of the maturity of the data. The ERG explained that because follow up occurs at specific intervals, Kaplan–Meier curves have a 'stepped' nature. This means that at each measurement, all people who have died or whose condition has progressed will leave the health state at once. The ERG explained that this may introduce bias into the modelling of survival outcomes for the blended comparator arm, and considered it more appropriate to use parametric modelling. The ERG base case used a Weibull curve to represent overall survival and a log-logistic curve to represent progression-free survival in the blended comparator arm. At technical engagement, the company did scenario analyses using parametric modelling to represent the blended comparator arm. The company explained that these scenarios had a minimal impact on the model results. NICE Decision Support Unit Technical Support Document 14 states 'parametric models are likely to represent the preferred method for incorporating survival data into health economic models in the majority of cases'. Based on this, the committee concluded that it was more appropriate to use parametric modelling to represent survival in the blended comparator arm.

It is appropriate to base time on treatment on CHRYSALIS time to treatment discontinuation data, extrapolated using the exponential curve

3.13 The company base case modelled time to treatment discontinuation based on the duration of progression-free survival. The company explained that this was because it was expected that people having amivantamab would stop treatment at progression. It also explained that because of closer monitoring, progression during the CHRYSALIS trial was likely to have been detected earlier than it would be in clinical practice. This could mean that the base-case approach underestimated

the benefits of amivantamab. The ERG noted that treatment duration with amivantamab during the CHRYSALIS trial was longer than progression-free survival. So, it considered that the company approach likely reduced estimated costs without reducing estimated effectiveness after progression. The ERG explained that their approach is to use the CHRYSALIS time to discontinuation data, with an exponential curve applied to model time on treatment. At technical engagement, the company provided a smoothed hazard curve for time to treatment discontinuation and explained that the hazard does not remain constant over time, instead decreasing initially before increasing from around month 5. The company considered this was most in line with the Weibull and Gompertz curves. It therefore provided a scenario analysis using the CHRYSALIS time to treatment discontinuation, with the Gompertz curve applied. The ERG explained that the Gompertz curve has the lowest number of people on treatment over time and only the fourth best statistical fit. The exponential curve (used in the ERG base case) had the best statistical fit. The company also provided an alternative scenario at technical engagement, which assumed that 50% of all people, regardless of treatment arm, stopped treatment at progression. This was in order to approximate a time on treatment somewhere between the company and ERG base case. The ERG noted that this scenario involved additional assumptions, which would require further validation. One of the clinical experts suggested that, on average, people are likely to continue having amivantamab for 2 to 3 months after disease progression, although this will vary widely. Overall, the committee concluded that it was appropriate for time on treatment to be based on the CHRYSALIS time to treatment discontinuation data, with the exponential curve (as the best statistical fit) applied.

It is appropriate to exclude treatment effect waning from the modelling

3.14 The company base case assumed that the amivantamab treatment effect is continued throughout the time horizon. The company said that because

people with exon 20 insertion mutation-positive NSCLC have poor prognosis with a short life expectancy, treatment effect waning is unlikely to be seen. And if treatment waning was experienced, it would be highly unlikely to have a clinically meaningful impact because of the short time periods over which it could occur. The company highlighted that overall survival data demonstrated that treatment benefit was maintained at follow up, and that clinician input confirmed that outcomes at 2 years and 5 years were aligned with their expectations. The ERG considered that there is limited evidence to support a lifelong treatment effect of amivantamab. At technical engagement, the company provided a scenario in which it applied linear treatment waning from 3 years after amivantamab treatment was stopped until efficacy was equal to that of the blended comparator arm. The company explained that this was consistent with the approach taken in NICE's technology appraisal guidance on nivolumab for treating advanced non-squamous non-small-cell lung cancer after chemotherapy. One of the clinical experts considered amivantamab's treatment effect is likely to be somewhere between that of existing oral EGFR TKIs (which provide little benefit after progression) and immunotherapies (which may provide long-term benefit). The committee noted that waning has typically been applied in previous appraisals for immunotherapies when stopping rules have been applied. It also noted the limited impact of the treatment-effect waning scenario done by the company. Based on this, the committee concluded that it was appropriate to exclude treatment effect waning from the modelling.

Costs in the economic model

Exon 20 insertion mutation testing costs should be included in a scenario analysis

3.15 In line with section 5.9.1 of NICE's guide to the methods of technology appraisal, the NICE scope for amivantamab states that the 'costs associated with diagnostic testing in people with NSCLC who would not

otherwise have been tested should be included' in modelling. The company did not include exon 20 insertion mutation testing in the economic modelling for amivantamab. It explained that these costs were expected to be included in routine NHS testing. The Cancer Drugs Fund lead explained that the gold standard for detecting exon 20 insertion mutations is next generation sequencing. But the availability of this varies across the NHS. Many treatment centres use polymerase chain reaction (PCR) instead, which is expected to identify about 50% of people with exon 20 insertion mutation-positive NSCLC. Because of this, using amivantamab (or other exon 20 insertion mutation-targeted treatments) in the NHS would mean switching from current local PCR testing to next generation sequencing at Genomic Laboratory Hubs. This could result in a 50% increase detecting exon 20 insertion-mutation-positive NSCLC. But the Cancer Drugs Fund lead suggested that this increase may only be 33%, because there is already some next generation sequencing testing being done. They explained that it would be appropriate to add a testing cost of £550 per person with exon 20 insertion mutation-positive NSCLC. This cost would account for a 2% incidence of exon 20 insertion mutations and the standard cost of adding a mutation test onto a next generation sequencing panel of £34. The committee concluded that it would be appropriate to consider scenarios with additional testing costs in the economic modelling.

End of life

Amivantamab meets the criteria to be considered a life-extending treatment at the end of life

3.16 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's guide to the methods of technology appraisal. The company proposed that amivantamab met the criteria for being a life-extending treatment for people with short life expectancy (normally less than 24 months). Both the company's base

case and the model using the committee's preferred assumptions predicted a mean and median overall survival with current standard care of substantially less than 24 months (the exact values are considered confidential by the company and cannot be reported here). Having considered the survival data from the US real-world evidence, the committee concluded that amivantamab met the end of life criterion for short life expectancy. The company's and ERG's modelling suggested that amivantamab was associated with a gain in overall survival of substantially more than 3 months (the exact values are considered confidential by the company and cannot be reported here). The committee noted the uncertainty in the real-world evidence and model estimates previously discussed (see sections 3.6 and 3.8). It concluded that, despite the uncertainty, amivantamab met both of NICE's criteria to be considered a life-extending treatment at the end of life.

Cost-effectiveness results

Because of the uncertainty, an acceptable ICER would be substantially below £50,000 per QALY gained

3.17 NICE's guide to the methods of technology appraisal notes that, above a most plausible incremental cost effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted the high level of uncertainty in the company's model, specifically:

- the lack of direct comparative evidence
- the effect of evidence selection issues because of the lack of transparency around identifying real-world evidence sources
- the potential for residual confounding in the indirect treatment comparison

- the uncertainty around extent of bias because of a lack of detailed information on real-world evidence provenance and suitability
- the lack of a fully incremental analysis.

Because of this, the committee would expect an acceptable ICER to be around £20,000 per QALY gained. However, the committee also agreed that the end of life criteria applied to amivantamab, which allows it to consider ICERs of up to £50,000 per QALY gained. The committee agreed that, when taking into account the substantial levels of uncertainty associated with the company's approach, an acceptable ICER would be at the lower end of the range normally considered cost-effective. This means that when end of life weighting is applied, the maximum acceptable ICER was substantially less than £50,000 per QALY gained. It highlighted that this acceptable ICER was based on the substantial levels of uncertainty associated with the company's approach to using real-world evidence.

The range of cost-effectiveness estimates are all above £50,000 per QALY gained

3.18 The company's base-case ICER for amivantamab compared with the blended comparator arm was over £50,000 per QALY gained, when commercial arrangements for amivantamab and all the comparators were included. The committee considered the scenario including its preferred assumptions, which were:

- excluding EGFR TKIs from the blended comparator arm (section 3.2)
- using the IPW method for the indirect treatment comparison (section 3.8)
- using utility values from TA713 (section 3.10)
- using parametric modelling to represent survival in the blended comparator arm (section 3.12)
- modelling time on treatment based on the CHRYSALYS time to treatment discontinuation data (section 3.13)
- excluding treatment waning (section 3.14).

It noted that the ICERs for this scenario and for all other scenarios presented were above £50,000 per QALY gained, when commercial arrangements for amivantamab and all the comparators were included. The exact ICERs are commercial in confidence and cannot be reported here. The committee also recognised that none of the scenarios presented considered the additional testing costs for EGFR exon 20 insertion-mutation testing (section 3.15). These costs, if included, would likely increase the ICERs. It also noted the substantial uncertainty in all of the cost-effectiveness estimates, and concluded that it could not recommend amivantamab for routine use.

Cancer Drugs Fund

Amivantamab does not meet the criteria to be included in the Cancer Drugs Fund

3.19 Having concluded that amivantamab could not be recommended for routine use, the committee then considered if it could be recommended for treating exon 20 insertion mutation-positive NSCLC in 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 company thought that the Cancer Drugs Fund would allow observational data collection on baseline characteristics, overall survival, time to treatment discontinuation and subsequent therapies through the Systematic Anti-Cancer Therapy dataset. It also suggested that the Cancer Drugs Fund would allow data from NCRAS to be linked to other datasets, to increase the sample size of the real-world evidence available from NHS clinical practice. The company suggested that this may resolve the uncertainties with the US real-world evidence. The committee recalled that the main uncertainties in this appraisal related to the limitations of the company's approach to existing real-world evidence (including the real-world evidence selection issues to identifying real-world evidence sources; see section 3.5). The

Cancer Drugs Fund lead said that, because CHRYSALIS was mature, making amivantamab available in the Cancer Drugs Fund would not generate data that would resolve the main uncertainties. They suggested that it may be difficult to get relevant additional data from the NCRAS that would increase the sample size of the retrospective real-world evidence available from NHS clinical practice. The committee recalled that all plausible ICERs were above £50,000 per QALY gained, and were substantially higher than the maximum considered acceptable because of the uncertainty in this appraisal. The committee concluded that it is unlikely that Cancer Drugs Fund data collection would reduce the uncertainties and improve the cost-effectiveness estimate for amivantamab. So, amivantamab could not be recommended for use in the Cancer Drugs Fund.

Other factors

Amivantamab is innovative but all benefits are captured in the analysis

3.20 The committee considered amivantamab to be innovative because it represents a step-change in the treatment of exon 20 insertion mutation-positive NSCLC. The company did not present any evidence to suggest that there were additional benefits that were not captured in the QALY calculations. The committee recognised that amivantamab provides important benefits for people with exon 20 insertion mutation-positive NSCLC. But it did consider that there were no additional benefits that had not been captured in the QALY calculations.

There are no equality issues relevant to the recommendations

3.21 The company explained that exon 20 insertion-mutation NSCLC is associated with people who have never smoked and has a higher prevalence in people from an East Asian family background. It also noted that lung cancer is often associated with stigma, which may result in a delay in seeking diagnosis and treatments. This may mean initial treatment options are not effective. The company considered that this

stigma may be greater in people who have never smoked and people with an East Asian family background. Differences in prevalence cannot usually be resolved in a technology appraisal, although the committee can consider whether a specific equality issue has a significant impact on access to treatment. It also considered principle 9 of the principles that guide the development of NICE guidance and standards, which states that the committee should take into account that 'stigma may affect people's behaviour in a way that changes the effectiveness of an intervention and routine quality of life assessments may not capture the benefits of treatment'. The committee noted that there was no evidence suggesting an increase in stigma in people protected by equality legislation. Also, the recommendation for amivantamab is for the full population in the marketing authorisation. So, the committee agreed that its recommendation would not have a different effect on people protected by the equality legislation than on the wider population. The committee concluded that there were no relevant equality issues.

Conclusion

Amivantamab is not recommended

3.22 The committee concluded that amivantamab is not recommended for treating EGFR exon 20 insertion mutation-positive NSCLC after platinum-based chemotherapy. This was because of the uncertainties in the evidence and because all of the ICERs were above the range considered to be a cost-effective use of NHS resources when the end of life modifier was applied.

Megan John
Chair, appraisal committee
August 2022

4 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.

Fatima Chunara
Technical lead

Carl Prescott
Technical adviser

Louise Jafferally
Project manager

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