NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Sotorasib for previously treated KRAS G12C mutation-positive advanced non-small-cell lung cancer

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using sotorasib 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: February 2026

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- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using sotorasib in the NHS in England.

For further details, see NICE's technology appraisal and highly specialised technologies guidance manual.

The key dates for this evaluation are:

- Closing date for comments: 26 March 2026
- Second evaluation committee meeting: To be confirmed
- Details of membership of the evaluation committee are given in section 5

1 Recommendations

1.1 Sotorasib should not be used for treating KRAS G12C mutation-positive locally advanced or metastatic non-small-cell lung cancer (NSCLC) in adults:

- when the cancer has progressed on platinum-based chemotherapy or anti-PD-1/PD-L1 immunotherapy, or
- when these treatments are not tolerated.

1.2 This recommendation is not intended to affect treatment with sotorasib that was funded with managed access before final guidance was published. If this applies, NHS England and the company have an arrangement to make sure people who started treatment during the managed access period will continue to have sotorasib until they and their NHS healthcare professional consider it appropriate to stop.

What this means in practice

Sotorasib is not required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because there is not enough evidence to determine whether sotorasib is value for money in this population.

Why the committee made these recommendations

This evaluation reviews the evidence for sotorasib for previously treated KRAS G12C mutation-positive advanced NSCLC (NICE technology appraisal guidance 781). It also reviews new evidence collected during the managed access period, which includes evidence from clinical trials and from people having treatment in the NHS in England.

Usual treatment for KRAS G12C mutation-positive locally advanced or metastatic NSCLC in adults when the cancer has progressed on platinum-based chemotherapy or anti-PD-1/PD-L1 immunotherapy, or these treatments are not tolerated, is docetaxel.

Clinical trial evidence shows that sotorasib increases how long people have before their condition gets worse compared with docetaxel. Clinical trial and real-world evidence suggests that sotorasib may increase how long people live compared with docetaxel. But this is uncertain because of the limitations in the evidence and how the data was analysed.

There are uncertainties with the economic model, including:

- which clinical evidence should be used in the model
- how the long-term benefits of sotorasib are modelled
- sotorasib's quality-of-life benefits.

Because of the uncertainties in the clinical evidence and economic model, it is not possible to determine the most likely cost-effectiveness estimates for sotorasib. Further analyses are needed. So, sotorasib should not be used.

2 Information about sotorasib

Marketing authorisation indication

2.1 Sotorasib (Lumykras, Amgen) is indicated for 'the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic NSCLC, who have progressed on, or are intolerant to, platinum-based chemotherapy and/or anti PD-1/PD-L1 immunotherapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of sotorasib is £6,907.35 for a 30-day supply of 120 tablets, each containing 240 mg (excluding VAT; BNF online accessed February 2026).

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

Sustainability

2.5 Information on the Carbon Reduction Plan for UK carbon emissions for Amgen will be included here when guidance is published.

3 Committee discussion

The evaluation committee considered evidence submitted by Amgen, 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.

The condition

Details of condition

3.1 Non-small-cell lung cancer (NSCLC) is staged from 1A to 4B according to the size of the tumour, location of involved lymph nodes and the presence of distant metastases. NSCLC diagnosed as stage 3 (locally advanced) or stage 4 (metastatic) is advanced. People with locally advanced NSCLC commonly present with a cough. Other symptoms include shortness of breath, coughing up blood and pain. People with metastatic NSCLC may also have headaches, an enlarged liver, changes in mental health, weakness and seizures. KRAS is a protein that helps control normal cell growth and survival. KRAS is one of most frequently mutated genes in cancer, including lung cancer. KRAS mutations are linked with a poorer response to treatment and survival

outcomes. The committee concluded that advanced NSCLC can substantially affect health-related quality of life.

Clinical management

Comparators

3.2 The company positioned sotorasib as second- and third-line treatment for people with KRAS G12C mutation-positive advanced NSCLC whose cancer has progressed on, or who are intolerant to, platinum-based chemotherapy or anti-PD-1/PD-L1 immunotherapy, in line with the marketing authorisation. The company's clinical experts advised that an increasing majority of people in the NHS with NSCLC (without mutations for which there are targeted treatments) now have immunotherapy (alone or with platinum-based chemotherapy) as first-line treatment and few have immunotherapy at second line. Because of this, immunotherapies were not considered relevant comparators. The company explained that platinum-based chemotherapy is rarely used after first-line immunotherapy and so it was excluded as a comparator.

Sotorasib for previously treated KRAS G12C mutation-positive advanced NSCLC (NICE technology appraisal 781; TA781) included docetaxel and docetaxel plus nintedanib as comparators. The company's clinical experts and the EAG agreed that docetaxel plus nintedanib is no longer frequently used and that docetaxel is more commonly used alone. This was consistent with evidence from the UK Cancer Analysis System (CAS) database. The clinical experts acknowledged that there could be differences in treatments used across the country. But both confirmed that, in their practices, docetaxel plus nintedanib is used less frequently and that use was declining because of toxicities. So, the committee concluded that docetaxel was the only relevant comparator for this evaluation.

Clinical effectiveness

Data sources

3.3 In TA781, the main clinical-effectiveness evidence for sotorasib came from the CodeBreak 100 trial, an ongoing phase 1 and 2, single-arm, open-label trial of sotorasib in people with KRAS G12C mutation-positive locally advanced or metastatic NSCLC. After being recommended through the Cancer Drugs Fund (CDF), new evidence was collected as part of the managed access agreement. The key clinical evidence in the current evaluation came from the CodeBreak 200 trial and the England-based Cancer Analysis System Real World Evidence (CAS RWE) study. All studies included people with NSCLC who had had at least 1 prior treatment.

The CodeBreak 200 trial is an ongoing phase 3, multicentre, open-label, randomised controlled trial comparing sotorasib with docetaxel. The study is being done at 149 centres globally including the UK. The trial recruited 171 people to the sotorasib arm and 174 people to the docetaxel arm. All participants were KRAS G12C mutation positive. The primary outcome was progression-free survival (PFS). Secondary endpoints include overall survival (OS) and health-related quality of life (HRQoL). In the August 2022 data cut, there was a statistically significant improvement for sotorasib compared with docetaxel for PFS (hazard ratio [HR] 0.66, 95% confidence interval [CI] 0.51 to 0.86). A protocol change resulted in a significant reduction in the sample size of the trial. As a result, the trial was no longer powered to detect a statistically significant difference in OS. After adjusting for all treatment switching (switching that happened as per the trial protocol and off-protocol), a post-hoc 2-stage adjustment analysis showed an OS HR of 0.82 (95% CI 0.32 to 1.31).

CAS RWE was a comparative, retrospective cohort study that used

real-world evidence from the CAS database in England. CAS RWE included evidence from the Cancer Outcomes and Services Dataset (COSD), the Systemic Anti-Cancer Therapy (SACT) dataset, and the Molecular Diagnostics (MDx) dataset. The study included 394 people who had sotorasib and 1,271 people who had docetaxel. The primary objective of the study was to compare OS in people having sotorasib or docetaxel as second-line or later treatment. The secondary objective was to compare time to next treatment or death (TTNTD). Statistical analyses, including propensity score weighting and standardised mortality ratio weighting, were used to balance and weight baseline characteristics between treatment groups. After these adjustments, there was a statistically significant improvement in TTNTD (HR 0.567 [95% CI 0.49 to 0.66]) and OS (HR 0.63 [95% CI 0.54 to 0.75]). The committee concluded that the CodeBreak 200 trial suggested sotorasib improved PFS. It noted that the CAS RWE study suggested improvements in TTNTD and OS, but that there were some key uncertainties (see section 3.4).

Evidence source used to inform clinical-effectiveness inputs

3.4 The company used data from the non-randomised CAS RWE study to inform the clinical-effectiveness inputs (TTNTD [used as a proxy for PFS], OS, and time to treatment discontinuation or death [TTDD]) in the economic model. The company said that the CAS RWE data should be used in the model instead of CodeBreak 200 data because it had a larger sample size (n=757 compared with n=345), a longer follow-up (39 months compared with 24 months) and was based in England, whereas the CodeBreak 200 trial was done in 149 centres globally (including the UK). Because of protocol changes in CodeBreak 200, the trial was no longer powered to detect a statistically significant difference in OS (see section 3.3). During the trial, 59 people (34%) having docetaxel were allowed to switch to sotorasib instead. Although the company adjusted the OS results for treatment switching, it said it was

concerned the results did not align with those from the CAS RWE study and the US-based Flatiron real-world evidence study. So it preferred to use the CAS RWE data.

The EAG noted these points but preferred to use evidence from CodeBreak 200 to inform the clinical-effectiveness inputs in the economic model. The EAG acknowledged that during recruitment to the CAS RWE study and through statistical and sensitivity analyses, efforts were made to ensure the populations having each treatment were similar. But the CAS RWE study was not randomised and so was at risk of selection bias and confounding that cannot be fully addressed by adjustments. During technical engagement, the company provided a risk-of-bias assessment (ROBINS-1) that showed the study was at serious risk of bias. The EAG noted that the KRAS mutation status of most of the people having docetaxel in CAS RWE was unknown, although the impact of mutation status on treatment effect is unclear. The proportions of people with known and unconfirmed mutation status are considered confidential and cannot be reported here. The mutation status of some people in the sotorasib group was also unconfirmed. But because a KRAS G12C mutation was a requirement for having sotorasib, the committee was reassured that most people having sotorasib had the mutation. Also, using CodeBreak 200 data enabled alignment of sources in the EAG's base-case economic model for baseline characteristics, OS, PFS and TTDD.

The committee considered the strengths and limitations of both studies. It noted that there was a lack of detailed information about the adjustments for treatment switching. So, the committee was uncertain if the adjustments were appropriate. The committee also noted that a lack of detail about the propensity score analysis, that was done on the CAS RWE data, meant that the committee was unable to thoroughly assess if this analysis was suitable or robust. The committee requested

more detail about the company's approach to adjusting for treatment switching and about the propensity score analysis. The committee considered the differences in KRAS G12C mutation status between the docetaxel and sotorasib groups as a major limitation. The committee acknowledged the strengths of using the same evidence source to inform all clinical outcomes. In this case, it concluded that it would consider the most appropriate evidence source for each clinical efficacy input (see section 3.6, section 3.8 and section 3.10).

Economic model

Company's modelling approach

3.5 The company's model was in line with the model presented in TA781. The company used a partitioned survival model with 3 health states: progression-free, progressive disease and dead. The committee concluded that the model structure was acceptable for decision making.

Assumptions

Modelling approach to OS

3.6 The committee preferred to use the evidence from the CAS RWE study to inform the results of the sotorasib group. This was because it was based in England, so the results were likely to best reflect outcomes in the NHS, and it had longer follow-up than CodeBreak 200. But the committee had concerns about the results from the docetaxel group in CAS RWE. This was because KRAS mutation status is likely to be a significant predictor of people's prognosis. The mutation status was unknown for most people having docetaxel and so the results may not be relevant to the population being evaluated. The company acknowledged this limitation and explained that KRAS mutation status was unknown because the study included results before sotorasib was available, and so routine genetic testing for this mutation was not done. Docetaxel is a non-targeted therapy and so people with a range of

mutations can have it. Also, the clinical experts explained that after sotorasib was made available through the managed access agreement, if testing had confirmed the presence of a KRAS G12C mutation, those people would likely have been offered sotorasib. This means that the docetaxel group was more likely to include more people without a KRAS G12C mutation. The company provided a Kaplan–Meier plot showing the OS results of people who had docetaxel, separated by KRAS mutation status. The company suggested this analysis showed that KRAS mutation status may not impact how effective docetaxel is, and so the results from the docetaxel group are still relevant. The EAG agreed, although it noted the sample sizes of people by mutation status were small, and so the results of this analysis were unclear.

The committee considered that the CAS RWE study best reflected the absolute OS benefits of treatment, but not the relative benefit compared to docetaxel. The committee noted that although there were limitations to the OS results in CodeBreak 200, the relative treatment effect adjusted for treatment switching from CodeBreak 200 may be a more plausible relative estimate than that from CAS RWE. This was because CodeBreak 200 was a randomised trial, directly comparing sotorasib with docetaxel, and included the population of interest. The committee also recalled the uncertainties in the docetaxel group of CAS RWE. So, the committee concluded that exploring an approach using the CAS RWE study to inform the baseline curves for sotorasib and then applying the inverse of the relative treatment effect from the CodeBreak 200 trial would help with decision making.

Extrapolating OS

3.7 The committee's preferred approach to inform OS was not reflected in either the company's or EAG's economic models. The 3-year and 5-year sotorasib OS estimates provided by the EAG's clinical expert were 7% and 2%, respectively. For docetaxel, these were 5% and 2%,

respectively. These are lower than the estimates provided by both clinical experts during the meeting. They stated that, anecdotally, they expected 3-year and 5-year OS estimates to be similar to those from the company's base case, which used the CAS RWE study. The company considers these estimates to be confidential so they cannot be reported here. The committee noted that the OS data from CAS RWE for sotorasib provided good quality evidence. But until further analyses were done (see section 3.6), and a decision made about the evidence source used to inform OS, it could not decide on its preferred approach for extrapolating OS.

Modelling approach for PFS and TTNTD

3.8 The committee had concerns about the company's approach of using TTNTD from the CAS RWE study as a proxy for PFS. The committee noted that this was a strong assumption, particularly because the PFS results from CodeBreak 200 and TTNTD results from CAS RWE were very different, and because PFS is likely to be shorter than TTNTD. The committee also recalled its concerns about the results from people who had docetaxel, because of the high proportion of people with unknown mutation status. The committee decided it would prefer to consider 2 alternative approaches:

- The first approach was to use the CodeBreak 200 trial results to inform PFS. The committee agreed that the PFS results from CodeBreak 200 were of good quality, because the trial was a randomised controlled trial and powered to produce statistically significant results. The committee had concerns about using different evidence sources to inform the sotorasib baseline curves for PFS (CodeBreak 200) and OS (CAS RWE). But in this case, because it was uncertain if TTNTD was an appropriate proxy for PFS, it decided it may be reasonable to use CodeBreak 200 data to inform PFS in the economic model. The committee was also reassured because the OS results for sotorasib

were similar in CodeBreak 200 and CAS RWE. So, if the PFS results for sotorasib were available from CAS RWE, they may be similar to sotorasib PFS results from CodeBreak 200. The committee also noted that there were limited other options that were suitable for decision making given the limitations with CAS RWE.

- The second approach was to use sotorasib TTNTD from CAS RWE as a proxy for PFS, but with an adjustment applied. Analyses comparing PFS and TTNTD from CodeBreak 200 could help explore the relationship between these outcomes. Then the sotorasib TTNTD data from CAS RWE could be adjusted to produce a better estimate of PFS in CAS RWE. Then, similarly to the modelling approach to OS, the inverse of the relative treatment effect for PFS would be applied to the sotorasib baseline curves to get the docetaxel curve. The committee noted that in CodeBreak 200, people were allowed to continue having sotorasib after disease progression. This could impact the true relationship between PFS and TTNTD. But, the committee agreed that these analyses would still be informative for decision making.

The committee requested that the company explore these 2 approaches as further analyses to understand the impact on the clinical and cost-effectiveness results. They should be combined with the approach suggested by the committee for OS (see section 3.6). The committee concluded that these analyses would help decide the most appropriate way to model PFS.

Extrapolating PFS and TTNTD

3.9 The committee's preferred evidence source for informing PFS was not reflected in either the company's or EAG's economic models. The different extrapolating approaches used by the company and EAG had a small impact on the cost-effectiveness results. But the committee noted that this was likely because of the way utilities were modelled. The

committee said that until further analyses were done, and a decision is made on the evidence source used to inform PFS, it could not decide on its preferred approach for extrapolating PFS.

Modelling approach to TTDD

3.10 For TTDD, the company preferred to use CAS RWE to align sources used to inform the clinical-effectiveness outcomes. The EAG's preferred approach was to inform TTDD directly by fitting parametric survival curves to the observed TTDD data from CodeBreak 200. The EAG requested this at clarification, but the company did not provide it. Without this analysis, the EAG used time-varying hazard ratios from CodeBreak 200 to inform TTDD in its base case. The committee asked the company to provide the requested analysis to aid its decision making.

Modelling relative treatment effect waning

3.11 In TA781, the committee concluded that it was plausible that there would be a waning of the relative treatment effect between sotorasib and docetaxel between 3 and 5 years after starting treatment. For the current evaluation, the company did not include an additional explicit waning assumption in the economic model. It said this was because the follow-up duration from the CAS RWE data was long enough to implicitly capture any treatment effect waning. The EAG stated that this was a strong assumption, especially as the log-cumulative and smoothed hazard plots for OS (from CodeBreak 200) showed converging curves, which may suggest waning. The EAG preferred to incorporate an explicit waning assumption, in which the relative OS gradually waned between 2 and 5 years after starting treatment. The committee noted that the method of modelling treatment effect waning had very little impact on the cost-effectiveness estimates. The committee said that because it had not decided on the approach to

extrapolate OS, it could not conclude if the waning assumption was appropriate.

Utility values

Source of utility values and mapping function

3.12 The company used HRQoL data from the EQ-5D-5L questionnaire from CodeBreak 200. The results from the questionnaire were mapped onto the EQ-5D-3L to align with the NICE reference case. But, this was mapped using the van Hout mapping function, rather than the Hernandez-Alava mapping function, as stipulated in the NICE reference case. The company preferred using the van Hout mapping function because the Hernandez-Alava function produced higher utilities, which the company thought to be inflated. The company stated this was an artefact of the Hernandez-Alava function and said that this was consistent with findings reported in a study by Maervoet and Bergemann (2024). The EAG preferred to use the Hernandez-Alava function in its base case because this aligned with the NICE reference case. Using the Hernandez-Alava mapping function had a small impact on the incremental cost-effectiveness ratio (ICER). The committee concluded it preferred to use the Hernandez-Alava mapping function stipulated in the NICE reference case.

Approach to modelling utility values

3.13 The company estimated utility values by descriptively analysing the HRQoL data by grouped time periods. This was used to inform its time-to-death (TTD) approach. The EAG preferred a progression-based approach to estimate utilities in line with the health states in the model. The company explored different mixed effects models for repeated measures (MMRM) to model utility. But the company did not provide an MMRM that included both progression and TTD covariates, as requested by the EAG. Instead, the company used a continuous TTD approach. Without this analysis, the EAG adopted the company's

approach to estimating utilities in the base case, with the exception of using the Hernandez-Alava mapping function (as discussed in section 3.12). Utilities in the EAG's and company's base cases were capped at UK general population values, adjusted for age and sex.

The company stated that it had considered the EAG's request, but to implement the TTD approach fully, it would have needed to explore all covariates, which was complex. It also noted that this could not be incorporated in a cohort state model and that doing so would introduce more uncertainty than it resolved. The committee acknowledged the company's concerns but noted that providing the MMRM the EAG requested would still be useful to explore the interaction between treatment and progression status.

The company used different utility values depending on the treatment people had. The company explained that this was because people having sotorasib have fewer treatment-related adverse events and the administration method is less burdensome than for docetaxel. The EAG considered this was sufficiently justified. This was because the MMRMs that included the treatment covariate had better statistical fit. The committee agreed that it was appropriate to use treatment-dependent utilities while people were progression-free. But it noted that the company's approach to modelling utilities implied that the lower utility value associated with docetaxel was applied for the whole time horizon, even after people stopped having docetaxel. The clinical experts said that the side effects from sotorasib were usually quickly reversible, whereas the side effects from docetaxel may take weeks. But they explained that once the side effects had stopped, they would expect the utility for people who had had either treatment to be the same after disease progression. So the committee asked the company to provide the MMRM with both progression and TTD covariates to help with decision making. The committee also noted that if the TTD approach is

used, it should be limited to 6 months before death. In the absence of this MMRM, the committee thought that treatment-independent utilities may also provide a useful estimate.

Costs

3.14 For the costs to administer docetaxel, the company had used the total unit costs, which is an average of the different ways and settings that docetaxel is administered. The clinical experts explained that docetaxel is usually administered as a day case. So the committee noted that it would like to see the economic model updated using day case unit costs for the administration of docetaxel.

Severity

3.15 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a greater weight to quality-adjusted life years (QALYs; a severity modifier) if technologies are indicated for conditions with a high degree of severity. The company provided absolute and proportional QALY shortfall estimates in line with NICE's technology appraisal and highly specialised technologies guidance manual. The absolute and proportional QALY shortfall estimates were dependent on the evidence source used to inform baseline characteristics and clinical efficacy inputs to calculate QALYs. The company preferred to use CodeBreak 200 data to inform the baseline characteristics and CAS RWE data to inform the efficacy inputs. The EAG preferred to align the evidence sources and so used CodeBreak 200 to inform baseline characteristics and efficacy. This was also consistent with the EAG's preferred model inputs discussed in section 3.4.

In CodeBreak 200 the median age was 64 years and the mean ages for sotorasib and docetaxel were 63.4 and 63.6 years, respectively. The

absolute and proportional shortfalls were sensitive to the age used to calculate them:

- In the company's base case, using a mean age of 63 resulted in a proportional shortfall of 0.9510, indicating that a severity weighting of 1.7 should be applied to QALYs. Using the median age of 64 resulted in a proportional shortfall of 0.9495, indicating a severity weighting of 1.2.
- In the EAG's base case, when using the median age of 64, absolute shortfall was 10.6 and proportional shortfall was 0.9397, indicating that a severity weighting of 1.2 should be applied.

The committee preferred to use the CAS RWE baseline characteristics for the absolute and proportional shortfall calculations because they best reflect the populations in the NHS. It considered the terminated technology appraisal 1076 (TA1076), which was for the same indication. In TA1076, the company and the EAG applied a severity of weighting of 1.7. But the committee noted that, in TA1076, OS data had been immature and so results and QALYs gained were uncertain. So in this current evaluation the committee stated that once additional analyses have been provided, it would be able to select an appropriate evidence source to inform the clinical-effectiveness inputs (see section 3.6, section 3.8 and section 3.10) and an appropriate approach to modelling utilities (see section 3.12). This would then inform the absolute and proportional shortfalls.

Cost-effectiveness estimates

Company and EAG cost-effectiveness estimates

3.16 The company base-case cost-effectiveness estimates were within the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained). The EAG's base-case estimates were

above this range. The committee was unable to choose an acceptable ICER because further analyses were needed from the company.

Committee's preferred assumptions

3.17 The committee concluded that the company's overall model structure was acceptable for decision making (see section 3.5). But because of the many areas of uncertainty, the committee could not decide on its preferred assumptions and requested further analyses from the company (see section 3.18).

Additional analyses

3.18 The committee noted the many areas of uncertainty. It would like to see the following additional analyses and information:

- more detail about the company's approach to adjusting for treatment switching and about propensity score analysis (see section 3.4)
- to model OS, applying the inverse crossover adjusted relative treatment effect from CodeBreak 200 to the baseline curves of sotorasib from CAS RWE to generate the docetaxel curves (see section 3.6)
- to model PFS, 2 approaches (see section 3.8):
  - using PFS from CodeBreak 200 to inform PFS directly
  - exploring the relationship between PFS and TTNTD from CodeBreak 200 and using this to adjust the TTNTD curve. This should be applied to TTNTD from CAS RWE to produce a better estimate of PFS in CAS RWE. The relative PFS efficacy from CodeBreak 200 should be applied to the sotorasib baseline curve to get the docetaxel curve.
- to model TTDD, extrapolating data from CodeBreak 200 (see section 3.10)
- to model utilities, providing an MMRM that includes both progression and TTD covariates. TTD should be limited to 6 months before death.

Alternatively, using treatment-independent utilities may also provide a useful estimate (see section 3.13).

- using day case unit costs for the administration of docetaxel (see section 3.14).

Equality

3.19 The committee noted that patient experts said that some people in this population may have cognitive impairments or disabilities that mean they struggle with the self-administration of sotorasib. Disability is protected under the Equality Act 2010. But, the committee agreed this was not something that could be addressed in its recommendation. The committee was mindful of its duties under the Equality Act 2010 and it identified another factor that should also be considered: not everyone is tested for KRAS mutations and so there could be inequalities in access to sotorasib across the NHS. But it decided that because its recommendation does not restrict access to treatment for some people over others, the committee agreed this was not an equalities issue.

Conclusion

Recommendation

3.20 The clinical-effectiveness evidence suggested that sotorasib improved key outcomes in people with KRAS G12C mutation-positive locally advanced or metastatic NSCLC whose disease has progressed on, or who cannot tolerate, platinum-based chemotherapy or anti-PD-1/PD-L1 immunotherapy. But there are some uncertainties in the clinical-effectiveness data and the economic model. The committee decided that, based on the analyses it had seen, it could not determine the most likely cost-effectiveness estimates for sotorasib. Given this uncertainty, the committee would like to see additional analyses (see section 3.18). So, sotorasib could not be recommended because there was not

enough evidence to determine whether sotorasib is value for money in this population.

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 B.

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

Baljit Singh

Chair, technology appraisal committee B

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 or principal technical adviser.

Enna Christmas

Technical lead

Alex Filby

Technical adviser

Kate Moore

Project manager

Elizabeth Bell

Principal technical adviser

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