NICE National Institute for Health and Care Excellence

NICE guidance

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

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Sotorasib is recommended for use within the Cancer Drugs Fund as an option for treating KRAS G12C mutation-positive locally advanced or metastatic non-small-cell lung cancer in adults whose disease has progressed on, or who cannot tolerate, platinum-based chemotherapy or anti-PD-1/PD-L1 immunotherapy. It is recommended only if the conditions in the managed access agreement for sotorasib are followed.

1.2 This recommendation is not intended to affect treatment with sotorasib 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 previously treated KRAS G12C mutation-positive, locally advanced or metastatic non-small-cell lung cancer includes docetaxel or docetaxel plus nintedanib. Sotorasib is a targeted treatment for the KRAS G12C mutation.

Sotorasib has only been indirectly compared with current treatment. The results suggest that, after platinum-based chemotherapy, sotorasib increases the time before the cancer gets worse and how long people live compared with current treatment.

Sotorasib likely meets NICE's criteria to be a life-extending treatment at the end of life. But there is uncertainty in the clinical evidence. Sotorasib has the potential to be cost effective, but more evidence is needed to address the uncertainties before it can be recommended for routine use.

The evidence on sotorasib is promising. But, more data is being collected from the primary clinical trial and from an ongoing randomised controlled trial comparing sotorasib with docetaxel. Collecting additional data through the Cancer Drugs Fund may resolve some uncertainty in the clinical evidence. So, sotorasib is recommended for use in the Cancer Drugs Fund.

2 Information about sotorasib

Anticipated marketing authorisation indication

2.1 Sotorasib (Lumykras, Amgen) is indicated 'as monotherapy for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small-cell lung cancer (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 anticipated list price of sotorasib is £6,907.35 for a 30-day supply of 240 tablets, each containing 120 mg (excluding VAT, company submission). The company has a commercial arrangement (managed access agreement including a commercial access agreement). This makes sotorasib 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 Amgen, 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.

The condition

There is a high unmet need for targeted treatments for KRAS G12C mutation-positive locally advanced or metastatic NSCLC

3.1 The KRAS oncogene is the most commonly mutated gene in lung cancer. The KRAS G12C mutation is the most common and occurs in 12% of non-small-cell lung cancer (NSCLC) tumours in the UK. This mutation is more common in non-squamous NSCLC and does not usually occur with other known mutations such as EGFR, ALK and ROS-1. These other known mutations may have targeted treatments available but there is currently no targeted treatment for the KRAS G12C mutation. People with KRAS G12C mutation-positive locally advanced or metastatic NSCLC usually have chemotherapy, a non-targeted treatment associated with adverse effects that affect health-related quality of life. The clinical expert highlighted that people with KRAS G12C mutation-positive NSCLC have a poor prognosis. The clinical and patient experts noted that there is an unmet need for effective and tolerable treatments in this population. They also highlighted that the lack of targeted treatment options can have a psychological impact. This condition is associated with difficult-to-treat symptoms, and the patient expert submission emphasised the psychological impact of these on patients and their carers. The clinical and patient experts stated that a targeted treatment for the KRAS G12C mutation in NSCLC would be welcomed. The committee concluded that there is an unmet need for targeted treatments for KRAS G12C mutation-positive locally advanced or metastatic NSCLC, and that these would have physical and psychological benefits.

Treatment pathway

Sotorasib is positioned after platinum-based chemotherapy, so docetaxel and docetaxel plus nintedanib are relevant comparators

3.2 The clinical experts explained that most people with untreated locally advanced or metastatic NSCLC would be offered immunotherapy with chemotherapy. Treatment with docetaxel or docetaxel plus nintedanib may be offered if the disease progresses. The clinical lead for the Cancer Drugs Fund highlighted that of all people with untreated locally advanced or metastatic NSCLC who have immunotherapy, about 40% have immunotherapy alone rather than with chemotherapy. In this population, platinum-doublet chemotherapy would be offered at disease progression, or through a clinical trial, before docetaxel or docetaxel plus nintedanib is considered. In its submission, the company chose to only compare sotorasib with docetaxel and docetaxel plus nintedanib. No evidence was provided to compare sotorasib with platinum-doublet chemotherapy. The company explained that 90% of people in the CodeBreaK100 trial (see section 3.3) had previously had platinum-doublet chemotherapy. Also, a retrospective UK analysis supported that most people who recently had docetaxel had likely had previous immunotherapy and platinum-doublet chemotherapy. The company stated that sotorasib is positioned in the treatment pathway after platinum-based chemotherapy. The clinical expert explained that platinum-doublet chemotherapy, either with or without immunotherapy, is usually the main treatment choice. The committee concluded that sotorasib is positioned after platinum-based chemotherapy, therefore docetaxel monotherapy and docetaxel plus nintedanib are the relevant comparators.

Clinical evidence

The clinical evidence for sotorasib is from CodeBreaK100, a phase 2, single-arm trial

3.3 The clinical effectiveness evidence for sotorasib is from the CodeBreaK100 trial. This is a phase 2, single-arm, multicentre, open label trial in 250 adults with KRAS

G12C mutation-positive advanced tumours; 126 participants had NSCLC. People in the trial previously had 1 (43%), 2 (35%) or 3 lines (22%) of anticancer therapy, measurable disease per RECIST 1.1 criteria and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Most people (90%) had previously had platinum-doublet chemotherapy (see section 3.2). People took 960 mg sotorasib (8 tablets of 120 mg) once a day until disease progression, treatment discontinuation or the end of the study. The primary outcome of the trial was an objective response rate of 37.1% (95% confidence interval 28.6 to 46.2), with the latest data-cut from March 2021. A pre-specified clinical significance benchmark of the lower bound of the 95% confidence interval excluding 23% was determined. The objective response rate was calculated as the sum of complete response (3.2%) and partial response (33.9%). This was assessed by a blinded independent central review per RECIST 1.1 criteria. The company noted that CodeBreaK100 was not specifically powered for overall and progression-free survival outcomes, but it was powered for the primary outcome. The committee acknowledged that the clinical evidence from the CodeBreaK100 trial is relevant.

Indirect treatment comparison

An indirect comparison is appropriate because there are no head-to-head trials with comparator treatments, but this increases uncertainty

3.4 There were no direct comparative data and no common trial arms for anchored indirect treatment comparisons or network meta-analyses. Therefore, the company used an unanchored indirect treatment comparison (as recommended in the NICE Decision Support Unit Technical Support Document 18) for sotorasib versus docetaxel and sotorasib versus docetaxel plus nintedanib. A matching-adjusted indirect comparison (MAIC) was used for the primary analysis of sotorasib versus docetaxel. Results from CodeBreaK100 were used for sotorasib. Results from SELECT-1, a randomised controlled trial comparing selumetinib plus docetaxel with docetaxel alone, were used for docetaxel. For the secondary analysis of sotorasib versus docetaxel plus nintedanib, the company regarded an MAIC as unfeasible. Therefore, a piecewise approach to hazard ratio estimates applied to the docetaxel arm of SELECT-1 was done using results from LUME-

Lung 1, a randomised controlled trial comparing docetaxel with docetaxel plus nintedanib. A supplementary analysis of sotorasib versus docetaxel was also done using a propensity score weighting analysis (PSWA) approach, using data from CodeBreaK100 for sotorasib and the chemotherapy arm of the Amgen Flatiron Health real-world evidence study. The committee concluded that an indirect treatment comparison is appropriate because there are no head-to-head trials, but noted there were several issues with the comparisons that introduced considerable uncertainty.

Sotorasib increases overall and progression-free survival compared with docetaxel and docetaxel plus nintedanib in the indirect comparison

3.5 The indirect treatment comparison showed that sotorasib is statistically superior in overall and progression-free survival compared with docetaxel. This was based on the latest March 2021 data-cut of the CodeBreaK100 trial (the exact results are confidential and cannot be reported here). The supplementary analysis supported these results. For the secondary analysis, the estimation of survival was implemented in the model and extrapolated over the time horizon. This showed a mean gain in overall and progression-free survival for sotorasib compared with docetaxel plus nintedanib (the exact results are confidential and cannot be reported here). The committee concluded that the indirect treatment comparisons show a survival benefit with sotorasib compared with docetaxel and docetaxel plus nintedanib.

The unanchored MAIC using SELECT-1 data is appropriate for decision-making but has substantial uncertainty

3.6 The company chose 4 covariates in the primary MAIC analysis for matching: ECOG performance score, mean age, metastatic disease at baseline and smoking status. These covariates were all perfectly matched to SELECT-1 (the exact results are confidential and cannot be reported here). Some covariates identified as 'very important' by clinical experts were excluded from matching by the company because of missing data or trial differences. The ERG noted that

excluding brain metastases affected prognosis identified by subgroup analysis. The company mentioned that active brain metastasis was excluded from the trials. The proportion of people with brain metastases was higher in CodeBreaK100 than in LUME-Lung 1. The company stated that if the proportion of inactive brain metastases in SELECT-1 was similar to CodeBreaK100, any bias would favour the docetaxel arm and result in conservative results. The ERG highlighted that an analysis including KRAS mutation status would be informative. But, it acknowledged the company's reasoning that overall survival and progression-free survival are similar in the absence of targeted therapies in the overall KRAS and KRAS G12C-specific population. However, it explained that it could have been possible to select KRAS G12C mutation data from SELECT-1 data. The ERG considered that the company's supplementary analysis using a PSWA may be less biased than the MAIC. It explained that the Amgen Flatiron Health real-world evidence data was adjusted to make it more comparable to the CodeBreaK100 population, and that there was little difference in the effective sample size compared with the MAIC. It also noted that the PSWA was adjusted for 13 covariates including brain metastases. However, the ERG highlighted that there remains considerable uncertainty in this approach. It noted that a PSWA limited to docetaxel-only data from the Flatiron study would have been informative. The committee agreed that using SELECT-1 instead of LUME-Lung 1 for the unanchored MAIC was appropriate. This is because the trial population was more comparable to CodeBreaK100, and it is also a more recent trial. The committee recognised that there are substantial uncertainties with this approach, but concluded that the primary analysis using SELECT-1 for the MAIC is appropriate for decision-making.

Docetaxel plus nintedanib modelling is uncertain, and applying a hazard ratio of 1 between 0 and 6 months is appropriate

3.7 In the secondary indirect treatment comparison of sotorasib versus docetaxel plus nintedanib, the ERG highlighted uncertainties in the modelling. The company modelled docetaxel and nintedanib in line with NICE's technology appraisal on nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. This was because a company-sourced UK advisory board confirmed that a MAIC was 'unlikely to be appropriate'. The ERG highlighted the uncertainty with not applying adjustments to ECOG, WHO or

smoking status when these differed in SELECT-1 and LUME-Lung 1. It also mentioned that the model's overall survival curve was not in line with the Kaplan–Meier curve in LUME-Lung 1, with an unlikely major increase in mortality in the first 6 months. That is, the modelling implied a worse survival for docetaxel plus nintedanib compared with docetaxel alone. The Kaplan–Meier curve showed a slight benefit of docetaxel compared with docetaxel plus nintedanib in the first 4 months, which then transformed into a greater than 1 year survival benefit for docetaxel in the modelled overall survival curves. The clinical expert mentioned that in clinical practice, docetaxel is not expected to be better than docetaxel plus nintedanib in the first 6 months. The clinical expert also highlighted that nintedanib has greater toxicity so more people may stop treatment earlier, but added that this is unlikely to be a major driver. The company suggested a possible explanation of the curve could be that nintedanib is anti-angiogenic, so it prevents the formation of blood vessels that support tumour growth. Therefore, it can take more time to have an effect and possibly explain the delay in survival. In addition, the ERG suggested using 1 cut-off point at 6 months rather than 2 at 6 and 26 months because this did not show a good fit. Therefore, the ERG preferred a hazard ratio of 1 between 0 to 6 months. The company disagreed with invalidating LUME-Lung-1, a 2-arm phase 3 trial. The committee highlighted the importance of face validity and concluded that there are uncertainties in the docetaxel plus nintedanib modelling, and that a hazard ratio of 1 between 0 and 6 months is appropriate.

Assumptions in the economic model

Treatment effect waning at 3 and 5 years from the start of treatment are plausible

3.8 The company did not apply treatment effect waning because it considered the impact of discontinuation on overall and progression-free survival to be implemented into the hazard function, and therefore, survival estimates. From the CodeBreaK100 March 2021 data-cut, 81.7% of people had discontinued treatment, about 40% were alive and about 20% had not yet progressed. The company stated that half the people who were alive will have kept taking sotorasib at that point. Because sotorasib is taken until progression or

unacceptable toxicity in CodeBreaK100, applying treatment effect waning could lead to biased cost-effectiveness estimates. The clinical expert suggested that it was difficult to know how the treatment effect waning should be applied for sotorasib. However, they suggested that sotorasib should be considered in a similar way to other oral treatments for NSCLC. The clinical lead for the Cancer Drugs Fund referred to an example of oral tyrosine kinase inhibitors showing high response rates. They noted that the disease can progress and people remain relatively well for some time before having symptoms. The clinical expert agreed with this. The company highlighted that sotorasib is not a tyrosine kinase inhibitor and that its mechanism of action and response rate would be different. The ERG disagreed with the company's assumption that sotorasib would have a continued benefit and highlighted that the evidence is still immature. In its base case, the ERG preferred to apply treatment effect waning at 2 years and gradually decrease the hazard ratio to 1 over 5 years. This was considered optimistic by the ERG. In addition, the ERG carried out additional scenario analyses with treatment effect waning at 3 and 5 years after starting treatment with no gradual decrease in the hazard ratio. This is in line with some other NSCLC appraisals. The committee noted that no direct trial evidence after the latest follow up at 15 months means that the treatment effect beyond this period is uncertain. The committee concluded that applying treatment effect waning 3 years and 5 years from the start of treatment may be plausible and it would consider these in its decision-making.

Health-related quality of life

Utility value estimates using the time-to-death and health-state approaches may be plausible

3.9 The company used time-to-death utilities in its base case and used health-state utilities as a sensitivity analysis. Although the ERG was not opposed to using time-to-death utilities, it preferred a health-state approach to utilities. This was because the ERG said that the time-to-death utilities did not seem well informed and they were comprised of a small sample size, especially near death. The committee understood that the health-related quality of life data was from the September 2020 data-cut, therefore it was more immature. The ERG noted that

the health-state utility approach means that each health state is populated with more people. The committee noted that for a health-state utility approach, the proportion of people in the progressed state that are closer to death are not apparent because averages are taken. The clinical expert highlighted that people need to be well enough to assess quality of life after progression. Therefore, the average is more likely representing people who recently stopped treatment. The committee considered that if a randomised controlled trial was done, the health-related quality of life in both arms should be the same at the start of treatment. Therefore, this may need to be considered in the approach to modelling health-related quality of life in the future. The company mentioned that it is open to using health-state utilities if there is a difference for sotorasib compared with chemotherapy after progression. The committee concluded that there are uncertainties in using time-to-death and health-state utilities, but because both approaches may be plausible, it would consider these in its decision-making.

Sotorasib is an oral treatment with associated benefits, and a disutility for the comparative intravenous treatment may be plausible

3.10 Sotorasib is an oral targeted treatment. It is more tolerable and less resource intensive than chemotherapy. The clinical expert described the issues associated with intravenous treatments, such as adverse events and delays in treatment because of capacity issues in chemotherapy units, particularly during the COVID-19 pandemic. The clinical expert highlighted the benefits of oral treatment from an NHS and patient perspective, and the preference for it. The patient expert described the benefits of having treatment at home and reducing inpatient time at the hospital. The company applied a utility decrement of 0.025 per cycle of treatment to account for the cytotoxicity and intravenous administration of docetaxel and nintedanib. This was based on a study comparing erlotinib with docetaxel in advanced NSCLC (Lewis et al., 2010). The utilities in that study were derived through a visual analogue scale in the progression-free health state. The ERG noted that the utilities (0.451 and 0.426 for oral and intravenous therapy, respectively) in that study were lower than in CodeBreaK100 (0.734). The ERG said it was not opposed to a treatment-related disutility for intravenous administration but highlighted the lack of justification for the size of disutility. It also considered the exclusion of any potential disutility associated with sotorasib

dosing and frequency as an issue. This is because sotorasib is taken as 8 tablets once a day compared with docetaxel that is administered intravenously once every 3 weeks. In its submission, the company assumed equal on-treatment progression-free survival utilities for a targeted therapy compared with chemotherapy. It acknowledged that a differential is seen in other NICE appraisals. The company identified a progression-free survival utility of 0.687 from LUME-Lung 1, resulting in a decrement of 0.047 after applying the progression-free survival base-case utility. As a result, the company determined that scenarios with a health-state utility approach and either 0.025 or 0.04 progression-free survival on-treatment utility differential were appropriate to explore. The committee concluded that it would consider both a disutility and no disutility associated with intravenous administration in its decision-making.

It is appropriate to apply an equalised relative dose intensity for sotorasib and its comparators

3.11 The company applied a relative dose intensity that was lower for sotorasib (89.0%) compared with docetaxel (90.3%) and nintedanib (92.1%). The company stated that there was no reason to assume that the relative dose intensity is truly lower for sotorasib, and any differences may be from random sampling errors. The ERG suggested it was reasonable to apply an average 90.5% relative dose intensity instead. The ERG preferred this conservative approach because of the impact on treatment costs and the immaturity of trial data. The company disagreed with equalised relative dose intensity because it considered the trial data more valid. The clinical expert mentioned that the dose of sotorasib can be modified depending on the level of unacceptable toxicity, whereas for chemotherapy, the maximum dose is normally applied. The committee noted that the proportion of people needing dose modifications in CodeBreaK100 was similar to SELECT-1. The committee concluded that it is appropriate to assume equalised relative dose intensities for sotorasib and its comparators.

End of life

Sotorasib may meet the end of life criteria but there is

uncertainty in the extension of life criterion

3.12 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 stated that for non-targeted therapies, real-world evidence studies suggest less than 10 months overall survival with second-line treatment and less than 7 months overall survival with third-line treatment. This was supported with a median overall survival of 7.9 months in SELECT-1 and median overall survival of 10.9 months in LUME-Lung 1. The committee accepted that sotorasib meets the short life expectancy criterion for end of life. It noted a median overall survival gain from the indirect treatment comparisons of sotorasib with docetaxel alone (see section 3.5) from the latest March 2021 data-cut, at around 15 months of follow up (the exact results are confidential and cannot be reported here). In addition, the model estimated an undiscounted mean overall survival gain for sotorasib compared with docetaxel and docetaxel plus nintedanib (the exact results are confidential and cannot be reported here). The committee agreed that sotorasib was likely to extend life by over 3 months and therefore meets the extension to life criterion. However, it noted that there were uncertainties with the unanchored indirect treatment comparison methods (see section 3.4). The committee concluded that sotorasib may meet both end of life criteria, but the length of life extension is uncertain.

Cost-effectiveness estimates

The most likely cost-effectiveness estimates are highly uncertain

3.13 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 and whether the technology meets the criteria for consideration as a 'life-extending treatment at the end of life'. 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 with an uncontrolled single-arm trial as the primary source of clinical

evidence (see section 3.3), the unanchored indirect treatment comparisons (see section 3.4), and other unresolvable issues. The committee outlined its preferred modelling assumptions with the current evidence, which should be applied to future cost-effectiveness analyses for sotorasib with docetaxel monotherapy and docetaxel plus nintedanib:

- initial hazard ratio of 1 between 0 and 6 months for docetaxel plus nintedanib modelling (see section 3.7)
- equalised relative dose intensity between treatment arms (see section 3.11)
- consideration of treatment waning effect at 3 and 5 years from the start of treatment (see section 3.8)
- consideration of time-to-death and health-state utilities (see section 3.9)
- application and non-application of disutility associated with intravenous administration (see section 3.10).

Sotorasib is not recommended for routine use in the NHS

3.14 The committee noted the uncertainties informing the cost-effectiveness estimates, including a single-arm trial as the primary clinical evidence and issues with the unanchored indirect treatment comparison. After applying confidential discounts for sotorasib and its comparators, and considering its preferences, the cost-effectiveness estimates were higher than what NICE normally considers an acceptable use of NHS resources. The cost-effectiveness results cannot be reported here because of the confidential discounts. The committee concluded it could not recommend sotorasib for routine use in the NHS.

Cancer Drugs Fund

Sotorasib is recommended for use in the Cancer Drugs Fund

3.15 Having concluded that sotorasib could not be recommended for routine use, the committee then considered if it could be recommended for treating previously

treated KRAS G12C mutation-positive locally advanced or metastatic 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 company has expressed an interest in the technology being considered for funding through the Cancer Drugs Fund. The clinical lead for the Cancer Drugs Fund mentioned that sotorasib needs to have plausible potential to be cost effective. The committee acknowledged that some of the clinical uncertainty may be addressed by collecting data on sotorasib through the Cancer Drugs Fund. The company explained that the phase 3 CodeBreaK200 trial, comparing sotorasib with docetaxel in a KRAS G12C mutation-positive population, is currently ongoing. It stated that this trial will measure overall and progression-free survival, and health-related quality of life. It will also collect data from people with previously treated disease. The committee agreed that some uncertainty may be resolved with data from the CodeBreak200 trial. The committee recalled its conclusion that the current cost-effectiveness results were highly uncertain. It agreed that, with longer follow-up data from CodeBreaK100 on mean overall and progression-free survival, and direct comparative evidence with docetaxel from CodeBreaK200, sotorasib has the potential to be cost effective. Also, that additional evidence may change the preferred modelling assumptions outlined in section 3.13. The committee concluded that sotorasib met the criteria to be considered for inclusion in the Cancer Drugs Fund. So, it recommended sotorasib for use within the Cancer Drugs Fund for previously treated KRAS G12C mutation-positive advanced NSCLC.

Other factors

There are no equality issues

3.16 No equality or social value judgement issues were identified.

Sotorasib has a novel mechanism of action in this treatment area, but all benefits are captured in the modelling

3.17 The patient and clinical experts emphasised the value of sotorasib as the first targeted treatment option for previously treated KRAS G12C mutation-positive, locally advanced or metastatic NSCLC. The committee considered the innovative nature of sotorasib (see section 3.1). It agreed that sotorasib could be considered an important treatment option for this population. The committee concluded that it did not think there were any additional benefits associated with sotorasib that had not been captured in the economic analysis.

Conclusion

Further data is needed to reduce uncertainties in the cost-effectiveness estimates, so sotorasib is recommended in the Cancer Drugs Fund

3.18 The committee considered all the available evidence for sotorasib in this appraisal. After considering its preferred modelling assumptions and NICE's end of life criteria, the committee concluded that sotorasib could not be recommended for routine use in the NHS. It considered that further follow-up data from CodeBreaK100 and direct comparative data with docetaxel from CodeBreaK200 may reduce some uncertainty in the cost-effectiveness estimates (see section 3.15). Therefore, sotorasib is recommended for use in the Cancer Drugs Fund for previously treated KRAS G12C mutation-positive advanced NSCLC.

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 previously treated KRAS G12C mutation-positive advanced NSCLC and the doctor responsible for their care thinks that sotorasib 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 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.

Abitha Senthinathan and Summaya Mohammad
Technical leads

Caron Jones
Technical adviser

Gavin Kenny
Project manager

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