

## sotorasib 120mg film-coated tablets (Lumykras®)

Amgen Ltd

4 February 2022

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

**ADVICE:** following a full submission assessed under the end of life and orphan equivalent process

**sotorasib (Lumykras®)** is accepted for use within NHSScotland on an interim basis subject to ongoing evaluation and future reassessment.

**Indication under review:** 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.

In a single-arm, phase II study, 37% of previously treated patients with advanced or metastatic, KRAS G12C-mutated NSCLC who received sotorasib achieved an objective response.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

**Chairman**  
**Scottish Medicines Consortium**

## Indication

As monotherapy 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.<sup>1</sup>

## Dosing Information

The recommended dose of sotorasib is 960mg (eight 120mg tablets) orally once daily, at the same time each day, with or without food. Treatment with sotorasib is recommended until disease progression or unacceptable toxicity.

The presence of a KRAS G12C mutation must be confirmed using a validated test prior to initiation of sotorasib therapy.

Dose modifications or interruption of dosing should be considered for the management of toxicities. See Summary of product characteristics (SPC) for more details.

Treatment must be initiated by a physician experienced in the use of anticancer medicinal products.<sup>1</sup>

## Product availability date

2 November 2021

Sotorasib received an Innovation Passport allowing entry into the Innovative Licensing and Access Pathway in February 2021.

Sotorasib meets SMC orphan equivalent and end of life criteria.

Sotorasib has conditional marketing authorisation from the Medicines and Healthcare Products Regulatory Agency.

## Summary of evidence on comparative efficacy

Sotorasib is an oral, selective KRAS G12C inhibitor which blocks tumour cell signalling and survival, inhibits cell growth and promotes apoptosis selectively in tumours harbouring KRAS G12C.<sup>1</sup>

The evidence supporting the efficacy and safety of sotorasib in NSCLC comes from CodeBreaK100, an ongoing, open-label, single-arm, phase I (dose escalation and expansion) and phase II study in patients with KRAS G12C-mutated advanced solid tumours, including NSCLC. Patients with NSCLC who were eligible to enrol in phase II were aged  $\geq 18$  years with a locally advanced or metastatic KRAS G12C-mutated NSCLC confirmed by a validated central test. They had disease progression after receiving anti-PD-1 or anti-PD-L1 immunotherapy or platinum-based chemotherapy or both, had measurable disease according to the Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 and an Eastern Co-operative Oncology Group (ECOG) performance status score of 0 or

1. During phase II, eligible patients were treated with sotorasib 960mg orally once daily, continued until disease progression, death, unacceptable toxic effects, or withdrawal of consent.<sup>2</sup>

The primary outcome was objective response rate (ORR, defined as a complete or partial response) assessed by blinded independent central review (BICR) and according to RECIST version 1.1 by contrast-enhanced computed tomography or magnetic resonance imaging. Efficacy analyses of response were performed in patients who had received at least one dose of sotorasib and had at least one measurable lesion at baseline when assessed by BICR using RECIST 1.1. SMC is unable to present the results of the primary outcome and secondary outcomes (duration of response, disease control rate, progression-free survival [PFS] and overall survival) at the primary analysis (cut-off date 1 September 2020). These results at two updated analyses (cut-off dates 1 December 2020 and 15 March 2021) are presented in Table 1.<sup>1-4</sup>

**Table 1: Results for the secondary outcomes in patients with KRAS G12C-mutated NSCLC in CodeBreaK100 at data cut-offs of 1 December 2020 and 15 March 2021<sup>1-4</sup>**

Data cut-off	Updated analysis	
	1 December 2020	15 March 2021
Number of patients	(n=124) <sup>1, 4</sup>	(n=124) <sup>2</sup>
Median duration of follow-up for ORR	NR	15.3 months
ORR by BIRC, % (95% CI)	37% (29% to 46%)	37% (29% to 46%)
Complete response, %	2.4%	3.2%
Partial response, %	35%	34%
Duration of response, months	10.0	11.1
Disease control rate by BIRC, % (95% CI)	81% (73% to 87%)	81% (73% to 87%)
Time to response, months	1.4	1.4
Median PFS by BIRC, months (95% CI)	6.8 (5.1 to 8.2)	6.8 (5.1 to 8.2)
Median duration of follow-up for overall survival, months	*	15.5
Median overall survival (n=126)	12.5 (10.0 to NE)	12.5 (10.0 to NE)

BIRC= blinded independent review committee; ORR=objective response rate; CI=confidence interval; PFS=progression-free survival; NR=not reported; NE=not estimable.\* SMC is unable to present this result

The submitting company presented indirect evidence comparing sotorasib with docetaxel monotherapy (which they considered the primary comparator) and with docetaxel plus nintedanib (which they considered the secondary comparator in adenocarcinoma). Comparison with docetaxel was performed via an unanchored matching adjusted indirect comparison (MAIC) using

individual patient level data for sotorasib from CodeBreaK100 and data for docetaxel from SELECT-1 (comparison of selumetinib plus docetaxel with docetaxel in patients with KRAS-mutated advanced NSCLC who had received one prior therapy).<sup>2, 6</sup> The outcomes compared were PFS and overall survival and results suggest that sotorasib was superior to docetaxel for both. In a confirmatory analysis, using docetaxel data from an analysis of the Flatiron real-world database performed by the company, the treatment effect for PFS for sotorasib versus docetaxel was smaller and indicated no evidence of a difference.

For the secondary comparison with docetaxel plus nintedanib, the company applied hazard ratios for PFS and overall survival from the difference between docetaxel versus docetaxel plus nintedanib from the LUME-Lung 1 study (adenocarcinoma patients of unknown KRAS mutation status) to the docetaxel arm of the SELECT-1 trial to provide an estimate of the relative treatment effects of sotorasib versus docetaxel plus nintedanib. The company propose that the results suggested sotorasib offers gains in PFS and overall survival.<sup>6, 7</sup>

*Other data were also assessed but remain confidential.\**

### Summary of evidence on comparative safety

CodeBreaK100 is a single-arm study and there are no comparative safety data. At the latest data cut-off (15 March 2021), the median duration of treatment with sotorasib was 5.5 months (range 0.2 to 17.8). Any treatment-emergent adverse event (AE) was reported by 99% (125/126) of patients and these were considered treatment-related in 70%. Patients reporting a grade 3 or higher AE was 58%, patients with a dose modification due to treatment emergent AEs was 22% and patients discontinuing therapy due to an AE was 7.1%. The most frequently reported treatment-emergent AEs of any grade with an incidence >15% in the sotorasib treated patients were: diarrhoea (51%), nausea (31%), fatigue (25%), increased alanine aminotransferase (21%) increased aspartate aminotransferase (21%), arthralgia (21%), constipation (19%), dyspnoea (19%), vomiting (18%), back pain (17%) and cough (15%).<sup>2</sup>

During CodeBreaK100, sotorasib was associated with increased alanine aminotransferase and/or aspartate aminotransferase and the SPC recommends that liver function is monitored before starting treatment, every 3 weeks for the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop transaminase and/or bilirubin elevations.<sup>1</sup>

Interstitial lung disease or pneumonitis was reported during CodeBreaK100 and occurred in patients treated with sotorasib with prior exposure to immunotherapy or radiotherapy. The SPC recommends that patients are monitored for new or worsening pulmonary symptoms indicative of interstitial lung disease or pneumonitis (for example dyspnoea, cough, or fever). Sotorasib treatment should be immediately withheld in patients with suspected interstitial lung disease or pneumonitis and permanently discontinued if no other potential causes are identified.<sup>1</sup>

## Summary of clinical effectiveness issues

The majority of lung cancers are diagnosed at an advanced stage and prognosis is poor. Approximately 85% to 90% of lung cancers are NSCLC of which there are three main subtypes: adenocarcinoma, squamous cell and large cell. KRAS mutations in cancer have been recognised for many years. The KRAS G12C mutation is the most common form of mutation in NSCLC and is estimated to occur in approximately 13% of all NSCLC cases. It is more common in non-squamous (adenocarcinoma and large cell) and rarer in squamous cell NSCLC. In lung cancer, KRAS mutations are more common in current or former smokers. Since there are no other treatments specifically available for KRAS G12C-mutated NSCLC, patients currently receive the same standard of care as NSCLC patients without an oncogenic driver with first-line treatment determined by PD-L1 status which may include platinum-based chemotherapy with or without pembrolizumab in patients with PD-L1 <50% or pembrolizumab monotherapy for patients with PD-L1 ≥50%. After standard first-line therapy, patients may receive docetaxel with or without nintedanib, platinum doublet therapy, pemetrexed or immunotherapy, depending on what has been used previously.<sup>8</sup> Patients eligible for sotorasib would have received previous treatment with platinum-based chemotherapy and/or anti-PD-1/PD-L1 immunotherapy and therefore the remaining relevant comparators include docetaxel with or without nintedanib. Sotorasib meets SMC orphan equivalent and end of life criteria.

### Key strengths

- In KRAS G12C-mutated NSCLC, patients who had previously been treated with platinum-based chemotherapy and/or anti PD-1/PD-L1 immunotherapy, treatment with sotorasib resulted in an ORR of 37%. ORR is an appropriate outcome to determine anti-tumour activity in a phase II study. This was supported by secondary outcomes of duration of response of 11.1 months, median PFS of 6.8 months and median overall survival of 12.5 months at the latest analysis (cut-off March 2021).<sup>2</sup>
- When indirectly compared with docetaxel and docetaxel plus nintedanib, sotorasib appeared to be associated with benefits in both PFS and overall survival.
- Sotorasib is the first medicine to be approved specifically for KRAS G12C-mutated NSCLC and offers the first targeted therapy for these patients.

### Key uncertainties

- Evidence is limited to 126 patients in a phase II, single-arm, open-label study, CodeBreak100, which is prone to various biases. Interpretation of the outcome data is limited by its uncontrolled nature. Response was assessed by BICR but the assessment of subjective outcomes such as quality of life and safety may be limited by the open-label design. The study is ongoing and final results are awaited.

- The generalisability of study results may be affected by the previous number of lines of therapy. In practice, targeted therapy with sotorasib may be more likely as early in the treatment pathway as possible (for example second-line). However, >50% of study patients had received two or three lines of previous therapy. Study patients had an ECOG performance score of  $\leq 1$  and the study results may not be generalisable to patients with poorer performance status in clinical practice.
- There are uncertainties concerning safety due to the lack of a control group during CodeBreak100. Longer term safety data are also awaited.
- There are no direct comparative data and no indirect comparative data with platinum doublet chemotherapy, which may be a relevant comparator in patients with PD-L1  $\geq 50\%$  who received immunotherapy alone in the first-line. Indirect evidence is presented versus docetaxel and docetaxel plus nintedanib. The MAIC suggested that sotorasib was superior to docetaxel in terms of PFS and overall survival. However there are a number of issues which limit the robustness of the analyses including the unanchored methods, differences between the study designs and populations and limited matching. The primary comparison was performed using a broader, not G12C specific, KRAS-mutated population for docetaxel, which in addition to differences between the studies in previous numbers of treatments and prior use of immunotherapy, were not adjusted for. The comparison with docetaxel plus nintedanib suggested that sotorasib offered a gain in PFS and overall survival. However the weak methods and differences between study populations, particularly comparison with docetaxel plus nintedanib using a general NSCLC population regardless of KRAS-mutation, limit the validity. There are limited data available for patients with KRAS G12C mutated NSCLC on which to base more robust indirect comparisons. Due to these limitations, the company's conclusions seem uncertain for the primary comparison with docetaxel and highly uncertain for the secondary comparison with nintedanib plus docetaxel.

The introduction of sotorasib may be associated with service implications, due to various monitoring requirements (including AST, ALT levels) although patient numbers are expected to be low. However, sotorasib is an oral medicine and offers an advantage in administration over intravenous medicines for patients and the service. Clinical experts consulted by SMC considered that sotorasib fills an unmet need offering a targeted treatment for patients with KRAS G12C-mutated NSCLC and is a therapeutic advance.

### **MHRA specific obligations<sup>9</sup>**

To assess the long-term effect of sotorasib in the indication under review, the marketing authorisation holder (MAH) is required to submit additional efficacy and safety follow-up data from the phase II, open-label study CodeBreak100 (due by June 2023).

To confirm the efficacy and safety of sotorasib in the indication under review, the MAH is required to submit the results from the multicentre, randomised clinical study CodeBreak200 (a confirmatory phase III comparative study with docetaxel) (due by July 2022).

To compare the safety and efficacy of sotorasib 960 mg daily versus a lower daily dose in a multicentre, randomised clinical study in patients with locally advanced or metastatic, KRAS G12C

mutated, non-small cell lung cancer who have received at least one prior systemic therapy (due June 2023). The specific obligations may address the key uncertainties in the clinical evidence presented.

Companion diagnostic required: contact local laboratory for information.

## Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of sotorasib, as an orphan equivalent and end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Advanced NSCLC is incurable and diagnosis is devastating for patients and their families. Progressive, debilitating symptoms include breathlessness, which can be very difficult to manage, fatigue, weight loss, and pain. These symptoms have a significant impact on patients' daily living and their quality of life.
- KRAS G12C is an uncommon mutation in patients with NSCLC. Compared with other mutation types in NSCLC, there are limited available treatment options and there is an unmet need for further effective and well-tolerated treatments. For some patients, the limited response and considerable toxicity make chemotherapy an unsuitable treatment option.
- Sotorasib offers the first targeted therapy for patients with KRAS G12C mutated NSCLC. In patients who respond, sotorasib may help control the disease, improve symptoms and offer patients and their family the hope of a better quality of life extension. Sotorasib may also offer efficacy in patients with brain metastases.
- Sotorasib is an oral treatment and generally has a manageable toxicity profile. The risk of serious/life-threatening toxicity or hospitalisation may be lower than expected with chemotherapy. These factors can reduce the burden of the disease and its treatment on patients, families and carers by allowing management in the home.

### **Additional Patient and Carer Involvement**

We received a patient group submission from the Roy Castle Lung Cancer Foundation, which is a registered charity. The Roy Castle Lung Cancer Foundation has received 12.5% pharmaceutical company funding in the past two years, including from the submitting company. A representative from the Roy Castle Lung Cancer Foundation participated in the PACE meeting. The key points of their submission have been included in the full PACE statement considered by SMC.

## Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis evaluating sotorasib within its full licensed indication. A comparison was provided against docetaxel, with a supplementary comparison provided against nintedanib and docetaxel. Clinical experts consulted by SMC suggest that docetaxel represents the most likely treatment to be displaced by sotorasib.

A standard three-state partitioned survival model was used, representing progression-free survival (PFS), post-progression survival (PD) and death. A separate partition was applied to represent the time spent on treatment. A lifetime horizon of 20 years was used, and a one-week cycle length applied.

In the base case, clinical data for sotorasib were derived from the CodeBreaK100 study<sup>2</sup>, which were then adjusted through the use of an unanchored MAIC to provide estimates of relative effectiveness versus docetaxel. After consideration of statistical goodness-of-fit, diagnostic plots and clinical input and external data, the submitting company applied a jointly-fitted restricted log-normal distribution to extrapolate overall survival for sotorasib and docetaxel. A jointly-fitted restricted log-normal distribution was also used to extrapolate progression-free survival for the two treatments. As a supplementary analysis, the submitting company also presented an analysis using adjusted data from the US Flatiron dataset. The treatment effect of sotorasib was assumed to be maintained across the time horizon, although a scenario was presented where the treatment effect equalises with docetaxel after five years. In the supplementary comparison with nintedanib and docetaxel, an additional piecewise Cox proportional hazards model was applied to estimate OS and PFS for the nintedanib regimen relative to the docetaxel data.

EQ-5D-5L data were collected within the CodeBreaK100 study and valued at an individual level using the van Hout et al 2012 crosswalk algorithm.<sup>10</sup> Health state utility values were then derived through use of a mixed model with repeated measures fitted to capture the utility associated with varying time periods before death (> 6 months: 0.76; 3 – 6 months: 0.72; 1 – 3 months: 0.64; <1 month: 0.53). Separate progression-based utilities were evaluated in a scenario analysis (PFS: 0.734; PD: 0.67). A disutility of 0.03 was applied for patients receiving intravenous treatment with docetaxel and disutilities were applied for select adverse events.

Costs of medicine acquisition were included for sotorasib and docetaxel, and an administration cost applied for docetaxel. A relative dose intensity (RDI) was applied for each medicine. Costs of sotorasib were applied on a daily basis, representing the cost per tablet rather than the cost per pack. Treatment duration for sotorasib was estimated using a Cox proportional hazards model, based on the observed hazard ratio of for treatment duration versus PFS from CodeBreaK100. Conversely, treatment duration for docetaxel and nintedanib plus docetaxel were assumed equal to progression. Health state-specific costs for PFS and PD included varying frequencies of outpatient attendances, CT scans and blood tests. One-off costs were also applied at disease initiation and upon progression, as well as for end of life care. The submitting company assumed that KRAS G12C testing is already routine practice within NHSScotland. No screening costs for this test were included despite it not currently being routinely available throughout NHSScotland.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a simple discount was offered on the list price.

The base case results for the comparison with docetaxel are shown in the table below. The main driver of the QALY gain for sotorasib is an increased life expectancy which results in more time spent with the “6+ months from death” utility applied, while the costs of medicine acquisition represent the key driver of incremental costs.

A range of sensitivity and scenario analyses were also presented, with the key scenarios summarised below.

**Table 1: Key scenario analyses with PAS**

	<b>Base case/Scenario</b>	<b>Base case approach</b>	<b>ICER (£/QALY)</b>
	<b>Base case</b>	<b>N/A</b>	<b>38,715</b>
1.	Use of Flatiron data for indirect treatment comparison	Use of unanchored MAIC	33,811
2.	15-year time horizon	20-year time horizon	39,696
3.	Log logistic distribution selected to estimate long-term OS and PFS projections	Log-normal distribution for OS and PFS projections	43,529
4.	MAIC-adjusted TTD curve from CodeBreak100	To test the impact of an alternative approach to estimate long-term treatment duration.	39,454
5.	HR of sotorasib vs. docetaxel = 1 after 5 years	Treatment effect of sotorasib maintained for time horizon	41,377
6.	Apply health state utilities by progression status	Use of time-to-death utilities	41,861
7.	Include drug wastage based on total packs administered (rather than days of tablets received)	Drug wastage based on days of tablets received	41,119
8.	Combined scenario	Combination of: 3, 5, 6, 7	50,079
OS, overall survival; PFS, progression-free survival; TTD, time to treatment discontinuation; HR, hazard ratio; MAIC, matching-adjusted indirect comparison; KM, Kaplan-Meier; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year;			

Although the modelling approaches were generally consistent with standard practice, there were a number of limitations relating to the methods and assumptions used:

- Given the single-arm nature of the CodeBreak100 study, an indirect comparison was necessary to estimate relative clinical effectiveness. Although a supplementary analysis was provided to support the base case approach, both analyses are subject to inherent uncertainties associated with indirect treatment comparisons. However, an ongoing randomised clinical trial is expected to provide greater certainty into the relative effects of sotorasib versus docetaxel.

- Although aligning with standard practice in survival extrapolations, the model selection process required some judgements in terms of the appropriateness of survival functions. While the submitting company selected one plausible survival function, others may be equally plausible (such as the log-logistic function). Scenarios utilising this alternative approach indicated some upwards sensitivity in the results (Scenario 3).
- The approach to modelling utilities made use of a time-to-death approach in the base case, with progression-based utilities used in a scenario analysis. While both approaches have been used in previous submissions, it may be appropriate to utilise both health-state specific (PFS and PD) utilities while applying time-to-death based disutilities. It was unclear what effect this approach would have on the ICER, however it was not expected to result in ICERs beyond those of the use of progression-based utilities alone (Scenario 6).
- An assumption of an ongoing treatment effect for sotorasib was considered potentially optimistic in the absence of longer-term or comparative data. An alternative scenario, where the effectiveness of sotorasib was assumed equal to docetaxel after five years, may be more appropriate and resulted in a slight increase in the ICER (Scenario 5).
- The costs of sotorasib were applied on a daily basis in the model, meaning that upon discontinuation of treatment any unused doses in a pack would not be wasted. For safety reasons, unused medications cannot be repurposed for other patients, and therefore this approach likely underestimated the total cost of sotorasib per patient. The use of costs on a 'per pack' basis resulted in an increased ICER (Scenario 7).
- When the above limitations were considered in combination, a more conservative but equally plausible combined scenario suggests that the ICER could fall higher than the base case estimate presented by the submitting company (Scenario 8). The Committee considered the benefits of sotorasib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted sotorasib for use in NHSScotland subject to ongoing evaluation and future reassessment.

### Additional information: guidelines and protocols

**The Scottish Intercollegiate Guidelines Network (SIGN)** published in 2014 the “Management of lung cancer”, a national clinical guideline.<sup>11</sup> This guidance is outdated and SIGN make no specific recommendations for patients with KRAS G12C-mutated NSCLC who have progressed on or are intolerant to platinum based chemotherapy and/or anti PD-1/PD-L1 Immunotherapy.

**The National Institute for Health and Care Excellence (NICE)** published in 2019 ‘Lung cancer: diagnosis and management’ (NICE guideline 122).<sup>12</sup> SIGN make no specific recommendations for patients with KRAS G12C-mutated NSCLC who have progressed on or are intolerant to platinum

based chemotherapy and/or anti PD-1/PD-L1 Immunotherapy. The guidelines recommend the use of docetaxel, docetaxel plus nintedanib, pembrolizumab, nivolumab or atezolizumab in the second line following previously failed treatment.

**European Society for Medical Oncology (ESMO)** published in September 2020 the clinical practice guidelines: 'Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up'.<sup>8</sup> For patients with KRAS G12C-mutated NSCLC, the guideline recommends that patients should be entered into a clinical trial.

The guideline makes the following recommendations for first-line treatment in the general management of NSCLC regardless of PD-L1 status:

- Chemotherapy with platinum doublets should be considered in all stage IV NSCLC patients without an actionable oncogenic driver, without major comorbidities and PS 0–2.
- Carboplatin plus nab-paclitaxel may be considered an option in advanced NSCLC patients, particularly in patients with greater risk of neurotoxicity, pre-existing hypersensitivity to paclitaxel or contraindications for standard paclitaxel premedication.
- platinum-based chemotherapy plus PD-(L1) inhibitors have reproducibly demonstrated superiority to standard platinum-based chemotherapy and in the absence of contraindications may be preferred to platinum-based chemotherapy in patients with PS 0 or 1 and PD-L1 < 50%.
- Pembrolizumab is considered a standard first-line option for patients with advanced NSCLC and PD-L1 expression  $\geq 50\%$  who do not have contra-indications to immunotherapy.
- Atezolizumab represents a promising first-line treatment option in patients with PD-L1-high NSCLC.
- Nivolumab plus ipilimumab represents an optional treatment regimen for patients with NSCLC.

The following recommendations are made for second-line treatment in the general management of NSCLC:

- In patients with progression after first-line immunotherapy with pembrolizumab, platinum-based chemotherapy is recommended as second-line treatment option.
- PD-L1 and PD-1 inhibitors (nivolumab, pembrolizumab and atezolizumab) are the treatment of choice for most patients with advanced, previously treated, PD-L1-naive NSCLC, irrespective of PD-L1 expression; nivolumab is recommended in both squamous and non-squamous NSCLC; pembrolizumab is recommended in patients with previously treated NSCLC with PD-L1 expression > 1%; atezolizumab is recommended in patients with advanced NSCLC previously treated with one or two prior lines of chemotherapy.
- in patients not suitable for immunotherapy, second-line chemotherapy is recommended. Options as second-line therapy consist of docetaxel, or nintedanib plus docetaxel in patients with adenocarcinoma progressing after previous chemotherapy or immunotherapy, ramucirumab plus docetaxel in patients progressing after first-line chemotherapy or

immunotherapy with PS 0–2.

- Erlotinib represents a potential second or third-line treatment option in particular for patients not suitable for immunotherapy or second-line chemotherapy in unknown EGFR status or EGFR wild type tumours.

These guidelines predate the availability of a targeted therapy for KRAS G12C mutation.

### Additional information: comparators

Docetaxel, docetaxel plus nintedanib.

### Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per 28 days (£)
sotorasib	960mg orally once daily	6,447

*Costs from Dictionary of Medicines and Devices Browser on 23 November 2021. Costs do not take patient access schemes into consideration.*

### Additional information: budget impact

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

[Other data were also assessed but remain confidential.\\*](#)

## References

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12. National Institute for Health and Care Excellence. Lung cancer: diagnosis and management. NICE guideline 122. Available at: <https://www.nice.org.uk/guidance/ng122>. 2019.

This assessment is based on data submitted by the applicant company up to and including 10 December 2021.

*\*Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: [http://www.scottishmedicines.org.uk/About\\_SMC/Policy](http://www.scottishmedicines.org.uk/About_SMC/Policy)*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

**Advice context:**

*No part of this advice may be used without the whole of the advice being quoted in full.*

*This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.*