NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Sotorasib for previously treated KRAS G12C mutation-positive advanced non-small-cell lung cancer (Managed Access review of TA781)

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of sotorasib within its marketing authorisation for treating previously treated NSCLC.

Background

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK, accounting for 12% of all new cancer cases and 19.5% of all cancer deaths between 2021.[1] Most lung cancers are diagnosed at an advanced stage when the cancer has spread to lymph nodes and other organs in the chest (locally advanced disease; stage 3) or to other parts of the body (metastatic disease; stage 4). Around 30% of lung cancers are diagnosed at an early stage (stage 1 or 2).[2]In 2022, 92% (around 34,000) of people diagnosed with lung cancer in England had NSCLC.[3]

KRAS is a protein that controls a signalling pathway crucial for cell growth, differentiation and survival. KRAS is the most frequently mutated oncogene in cancer, including lung cancer, with KRAS G12C mutation occurring in about 11% of NSCLC.[5] It is more common in non-squamous NSCLC, and relatively rare in squamous NSCLC.[6]

For untreated metastatic non-squamous NSCLC people may be offered pembrolizumab with pemetrexed and platinum chemotherapy (TA683) or pemetrexed and platinum chemotherapy irrespective of PD-L1 expression. If the non-squamous NSCLC expressed PD-L1 on less than 50% of tumour cells, people may be offered atezolizumab plus bevacizumab, carboplatin and paclitaxel (TA584) or pemetrexed with platinum doublet chemotherapy. If the non-squamous NSCLC expressed PD-L1 on over 50% of tumour cells they may be offered pembrolizumab (TA531) or atezolizumab (TA705) monotherapy.

For untreated squamous NSCLC people may be offered pembrolizumab with carboplatin and paclitaxel (TA770) if the NSCLC expresses PD-L1 on less than 50% of cells or on over 50% of cells if there is a need for urgent clinical intervention. If the squamous NSCLC expresses PD-L1 on less than 50% of its tumour cells people may be offered pembrolizumab (TA531) or atezolizumab (TA705) monotherapy.

For KRAS G12C positive NSCLC that has been previously treated sotorasib is recommended within the cancer drugs fund (TA781).

Alternatively docetaxel or docetaxel with nintedanib (TA347) may be offered as a second line treatment, irrespective of first-line treatment. If chemotherapy without immunotherapy was used as a first-line treatment, then people may be offered an immunotherapy monotherapy consisting of either nivolumab (TA655 & TA713), atezolizumab (TA520) or pembrolizumab (for PD-L1 positive disease, TA428). If an

immunotherapy monotherapy was used at first line, then people may be offered platinum-based chemotherapy as a second-line treatment.

This evaluation considers the managed access review of sotorasib (TA781).

The technology

Sotorasib (Lumykras, Amgen) has a marketing authorisation in the UK 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.

Intervention(s)	Sotorasib
Population(s)	Adults with previously treated KRAS G12C mutated, locally advanced or metastatic NSCLC.
Subgroups	If the evidence allows the following subgroups will be considered: • Disease stage • Histology • Previous treatment • Newly diagnosed or recurrent distant metastatic disease
Comparators	• Docetaxel • Docetaxel with nintedanib • Adagrasib (subject to NICE appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to treatment discontinuation • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account. The use of sotorasib is conditional on the presence of KRAS G12C mutation. The economic modelling should include the costs associated with diagnostic testing for KRAS G12C in people with NSCLC who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Sotorasib for previously treated KRAS G12C mutation-positive advanced non-small-cell lung cancer (2022) NICE technology appraisal guidance 781. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (2022) NICE technology appraisals guidance 770. Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer (2021) NICE technology appraisals guidance 683. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (2021) NICE technology appraisal guidance 705. Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy (2021) NICE technology appraisal guidance 713.

	Nivolumab for advanced squamous non-small-cell lung cancer after chemotherapy (2020) NICE technology appraisal guidance 655. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisal 584. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology appraisal guidance 531. Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) NICE technology appraisal guidance 520. Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (2017) NICE technology appraisal guidance 428. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer (2015) NICE technology appraisal guidance 347. **Related technology appraisals in development:** Adagrasib for previously treated KRAS G12C mutation-positive advanced non-small-cell lung cancer [ID6339]. In development. **Related NICE guidelines:** Lung cancer: diagnosis and management (NG122) **Related quality standards:** Lung cancer in adults (2019) NICE quality standard 17

Questions for consultation

Have all the relevant comparators for sotorasib been included in the scope?

Is the KRAS G12C mutation tested for as part of routine practice in advanced or metastatic NSCLC care?

Have all the relevant subgroups for sotorasib been included in the scope?

Do you consider that the use of sotorasib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

Where do you consider sotorasib will fit into the existing care pathway for locally advanced or metastatic NSCLC?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit

and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which sotorasib is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. NHS England (2024). Cancer Registration Statistics, England, 2022. Accessed February 2025.
2. Royal College of Surgeons of England (2024). National Lung Cancer Audit: State of the Nation Report 2024. Accessed February 2025.
3. Royal College of Surgeons of England (2024). National Lung Cancer Audit: Data and statistics. Data tables (Excel). Accessed February 2025.
4. Office for National Statistics (2019). Cancer survival in England – adults diagnosed. Cancer Survival in England: adults diagnosed between 2013 and 2017 and followed up to 2018 (Excel dataset). Accessed February 2025.
5. Reita D, Pabst L, Pencreach E et al (2022) . Direct Targeting *KRAS* Mutation in Non-Small Cell Lung Cancer: Focus on Resistance. Cancers (Basel). Mar 4;14(5):1321
6. Martin P, Leighl NB, Tsao MS and Shepherd FA (2013) KRAS mutations as prognostic and predictive markers in non–small cell lung cancer. Journal of Thoracic Oncology 8(5):530-542.