NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Sotorasib for previously treated KRAS G12C mutated, locally advanced or metastatic non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of sotorasib within its marketing authorisation for previously treated KRAS G12C mutated non-small-cell lung cancer.

Background

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK, accounting for 13% of all new cancer cases and 21% of all cancer deaths in 2017.[1] There are around 48,000 new lung cancer cases and 35,000 deaths from lung cancer in the UK every year. The majority of 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 III) or to other parts of the body (metastatic disease; stage IV). Up to 85% of lung cancers are non-small-cell lung cancers (NSCLC).[2] NSCLC may be grouped by tumour histology into squamous cell carcinoma, adenocarcinoma and large-cell carcinoma, with the latter 2 being collectively referred to as 'non-squamous' lung cancer.

KRAS is an enzyme 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 being responsible for about 12% of NSCLC.[3] It is more common in non-squamous NSCLC, and relatively rare in squamous NSCLC.[4]

The aims of treatment for advanced NSCLC are to prolong survival and improve quality of life. Currently, treatment choices are influenced by the presence of biological markers (such as genetic alterations in EGFR-TK, ALK or ROS1, or PD-L1 expression), histology (squamous or non-squamous) and prior treatments (NICE Lung cancer pathway). There are currently no treatments available that target KRAS G12C.

The technology

Sotorasib (proposed international non-proprietary name for AMG 510, Amgen Ltd) is a small molecule inhibitor of KRAS G12C protein, which locks it in an inactive state. This may block signalling between tumour cells and stop further growth. Sotorasib is given as an oral tablet.

Sotorasib does not currently have Marketing Authorisation in the UK for any indication. It is in clinical development for the treatment of adults with KRAS G12C mutated, locally advanced or metastatic NSCLC. It is intended to be used following prior standard therapy for NSCLC.

Intervention(s)	Sotorasib
Population(s)	Adults with previously treated KRAS G12C mutated, locally advanced or metastatic NSCLC

Comparators	Non-squamous NSCLC:
	• atezolizumab combination (after EGFR- or ALK-targeted therapies)
	• pemetrexed with carboplatin
	  o with or without pemetrexed maintenance
	• other platinum doublet chemotherapy
	  o with or without pemetrexed maintenance
	• nintedanib with docetaxel (adenocarcinoma histology)
	• docetaxel monotherapy
	• atezolizumab
	• nivolumab (subject to ongoing CDF review)
	• pembrolizumab (PD-L1-expressing tumours)
	• best supportive care
	Squamous NSCLC:
	• gemcitabine with carboplatin or cisplatin
	• vinorelbine with cisplatin or carboplatin
	• docetaxel monotherapy
	• pembrolizumab (PD-L1-expressing tumours)
	• atezolizumab
	• nivolumab
	• best supportive care

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 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 5.9 of the Guide to the Methods of Technology Appraisals'.
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 and NICE Pathways	**Related Technology Appraisals:** Nivolumab for previously treated squamous non-small-cell lung cancer (2020) NICE technology appraisal guidance 655 Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisal guidance TA584 Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) NICE technology appraisal guidance 520 Nivolumab for previously treated non-squamous non-small-cell lung cancer (2017) NICE technology appraisal guidance 484 [undergoing CDF review] Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (2017) NICE technology appraisal guidance TA428 Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer (2016) NICE technology appraisal guidance 403 Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016) NICE technology appraisal guidance 402 Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy (2015) NICE

	technology appraisal guidance 374 Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer (2015) NICE technology appraisal guidance 347 Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010 updated 2017) NICE technology appraisal guidance 190 **Terminated appraisals** Afatinib for treating advanced squamous non-small-cell lung cancer after platinum-based chemotherapy (terminated appraisal) (2017) NICE technology appraisal 444 **Appraisals in development** Selpercatinib for RET fusion-positive advanced non-small-cell lung cancer. NICE technology appraisal guidance. Publication date to be confirmed. Tepotinib for treating advanced non-small-cell lung cancer with MET gene alterations. NICE technology appraisal guidance. Publication date to be confirmed. **Related Guidelines:** Lung cancer: diagnosis and management (2019) NICE guideline NG122 **Related Quality Standards:** Lung cancer in adults (2019) NICE quality standard 17 **Related NICE Pathways:** NICE Lung cancer pathway: treating non-small-cell lung cancer
Related National Policy	**National Service Frameworks:** Cancer **Department of Health:** Department of Health, NHS Outcomes Framework 2016-2017: Domains 1, 2, 4, 5. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: Specialist cancer services (adults) **Other policies** Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020

Questions for consultation

Where do you consider sotorasib will fit into the existing NICE pathway for treating non-small-cell lung cancer?

- For non-squamous NSCLC with KRAS G12C mutation and no other known targetable genetic alterations (EGFR, ALK, ROS1)
- For non-squamous NSCLC with KRAS G12C mutation in addition to other known targetable genetic alterations (EGFR, ALK, ROS1)
- For squamous NSCLC

Have all relevant comparators for sotorasib been included in the scope, for all populations listed above?

How frequently KRAS G12C mutation coexists with other known targetable genetic alterations (EGFR, ALK, ROS1)? Is there any published evidence to support this estimate?

Are the outcomes listed appropriate? Are any key outcomes missing?

Are there any subgroups of people in whom sotorasib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 will be 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.

Do you consider sotorasib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of sotorasib can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Lung cancer incidence. Cancer Research UK. Accessed September 2020.
2. Types of lung cancer. Cancer Research UK. Accessed September 2020.
3. Herbst RS and Schlessinger J (2019) Small molecule combats cancer-causing KRAS protein at last. Nature 575(7782):294-295.
4. 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.

