NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Rociletinib for previously treated locally advanced or metastatic, EGFR T790M -positive non-small-cell lung cancer

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of rociletinib within its marketing authorisation for previously treated locally advanced or metastatic, EGFR T790M-positive non-small-cell lung cancer (NSCLC).

Background

Lung cancer falls into two main histological categories: around 85–90% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers. 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). People with NSCLC can be either epidermal growth factor receptor (EGFR)-positive or EGFR-negative and those with EGFR-positive disease can receive EGFR tyrosine kinase inhibitor (EGFR-TKI) treatment. A mutation can occur at the 790 position of the EGFR, T790M, causing resistance to EGFR-TKI treatment. The T790M mutation accounts for approximately 50% of EGFR-TKI resistance.[1]

In 2013, approximately 26,800 people were diagnosed with NSCLC in England, of whom 6500 (23%) had stage III and 13,000 (46%) had stage IV disease.[2] Lung cancer caused approximately 28,000 deaths in England in 2012.[3] The median survival with lung cancer (all stages) is approximately 6 months; 35% of people with lung cancer, survive for more than 1 year after diagnosis.[2]

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers (such as mutations in EGFR-TK, ALK or PD-L1 status), histology (squamous or non-squamous) and previous treatment experience. NICE clinical guideline 121 (CG121) recommends platinum-based chemotherapy as an option for people with previously untreated stage III or IV NSCLC and good performance status. Docetaxel monotherapy and nintedanib in combination with docetaxel are recommended as treatment options for patients with previously treated NSCLC in certain circumstances (NICE clinical guideline 121 and NICE technology appraisal guidance 347 respectively). Best supportive care may be considered for some people for whom chemotherapy is unsuitable or may not be tolerated.

The technology

Rociletinib (Xegafri, Clovis Oncology) is a targeted, covalent (irreversible) mutant-selective EGFR-TKI. It selectively targets both initial activating EGFR mutations and the T790M resistance mutation while sparing the wild-type or normal EGFR. It is administered orally.

Rociletinib does not currently have a marketing authorisation in the UK for previously treated locally advanced or metastatic, EGFR T790M-positive NSCLC. It is currently being studied in a clinical trial as monotherapy compared with single-agent chemotherapy (pemetrexed, gemcitabine, paclitaxel, docetaxel) in adults with EGFR positive, metastatic or unresectable locally advanced NSCLC, who have received at least 1 prior treatment with an EGFR-TKI.

Intervention(s)	Rociletinib
Population(s)	People with previously treated locally advanced or metastatic, EGFR T790M- positive non-small-cell lung cancer who have been previously treated with an EGFR-targeted therapy
Comparators	• docetaxel monotherapy • platinum therapy (in combination with gemcitabine, vinorelbine, pemetrexed or a taxane) • nintedanib in combination with docetaxel • best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 patient access schemes for the intervention or comparator technologies should be taken into account. If appropriate, the appraisal should include consideration of the costs and implications of additional testing for genetic markers, but will not make recommendations on specific diagnostic tests or devices.
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: Nintedanib for treating previously treated metastatic non-small cell lung cancer (2015) NICE Technology Appraisal 347. Related Guidelines: The diagnosis and treatment of lung cancer (2011). NICE guideline 121. Review date December 2015. Related Quality Standards: Quality standard for lung cancer. (2012). NICE Quality Standard No. 17 http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy	NHS England, Manual for prescribed specialised services, service 105: specialist cancer services (adults), Jan 2014. http://www.england.nhs.uk/wp-

	content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health (2013) Improving outcomes: a strategy for cancer, 3rd annual report Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf

Questions for consultation

Have all relevant comparators for rociletinib been included in the scope? How should best supportive care be defined?

Which treatments are considered to be established clinical practice in the NHS for previously treated locally advanced or metastatic, EGFR T790M-positive non-small-cell lung cancer?

Is T790M mutation testing routinely carried out in English clinical practice? If so, which CE marked diagnostic test is used?

Is single agent chemotherapy offered to patients whose disease has progressed despite treatment with a first EGFR-TKI therapy? If so, which treatments are given?

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

Where do you consider rociletinib will fit into the existing NICE pathway, lung cancer?

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 rociletinib will 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 rociletinib 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 rociletinib 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.

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. Su K, Chen H, Li K et al. (2012) Pretreatment epidermal growth factor receptor (EGFR) T790M mutation predicts shorter EGFR tyrosine kinase inhibitor response duration in patients with non–small-cell lung cancer. Journal of Clinical Oncology 2012;30(4):433-440.

2. National Lung Cancer Audit: 2013 Patient Cohort. Published 2014.

3. Cancer Research UK (2013) Lung cancer survival and mortality statistics. [accessed July 2015]