

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Proposed Health Technology Appraisal**

**Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer**

**Draft scope (pre-referral)**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of ramucirumab within its marketing authorisation for treating locally advanced or metastatic non-small-cell lung cancer that has progressed after platinum-based chemotherapy.

**Background**

Lung cancer falls into 2 histological categories: non-small-cell lung cancers, which account for 85–90% of all lung cancers, and small-cell lung cancers. Non-small-cell lung cancer may be further 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.

In England, there were 34,889 people newly diagnosed with lung cancer in 2011. Approximately 30% of people present with locally advanced disease (stage III; the cancer may have grown into the surrounding tissues and there may be cancer cells in the lymph nodes) and 40% with metastatic disease (stage IV; the cancer has spread to another part of the body). The prognosis for people with non-small-cell lung cancer is generally poor, with a 5-year survival rate of 9%. Approximately 28,300 deaths from lung cancer were registered in England in 2012<sup>1</sup>.

For most people with non-small-cell lung cancer, the aims of treatment are to extend survival and improve quality of life. For many people with stage IIIB or IV disease, the cancer has spread too far for surgery or radiotherapy to be effective, so chemotherapy is recommended. For people with previously untreated, stage III or IV non-small-cell lung cancer and good performance status, NICE clinical guideline 121 recommends chemotherapy with a platinum drug (carboplatin or cisplatin) in combination with a third-generation drug (docetaxel, gemcitabine, paclitaxel or vinorelbine). If subsequent treatment is appropriate, docetaxel monotherapy should be considered for people with locally advanced or metastatic non-small-cell lung cancer that has relapsed after previous chemotherapy (NICE clinical guideline 121). NICE technology appraisal 162 (which is currently being reviewed) also recommends erlotinib, as an alternative treatment option to docetaxel, for previously treated, non-small-cell lung cancer in people in whom docetaxel is suitable. Best supportive care is considered an option for people who are unlikely to tolerate chemotherapy.

### The technology

Ramucirumab (Cyramza, Lilly) is a fully human immunoglobulin G1 monoclonal antibody. It specifically blocks the vascular endothelial growth factor receptor-2, which plays an important role in angiogenesis (formation of new blood vessels) in tumours. Ramucirumab is administered intravenously.

Ramucirumab does not currently have a marketing authorisation in the UK for locally advanced or metastatic non-small-cell lung cancer. Ramucirumab plus docetaxel has been studied in clinical trials, compared with placebo plus docetaxel, in adults with stage IV non-small-cell lung cancer after disease progression on platinum-based therapy.

<b>Intervention(s)</b>	Ramucirumab in combination with docetaxel
<b>Population(s)</b>	People with locally advanced or metastatic non-small-cell lung cancer that has progressed after platinum-based chemotherapy
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Docetaxel</li> <li>• Erlotinib (subject to ongoing NICE review)</li> <li>• Best supportive care</li> </ul> <p>For people with adenocarcinoma tumour histology only:</p> <ul style="list-style-type: none"> <li>• Nintedanib in combination with docetaxel (subject to ongoing NICE appraisal)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rates</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

<p><b>Economic analysis</b></p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
<p><b>Other considerations</b></p>	<p>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.</p>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p>Related Technology Appraisals:</p> <p>‘Erlotinib for the treatment of non-small-cell lung cancer’ (2008). NICE Technology Appraisal 162. Currently under review.</p> <p>‘Pemetrexed for the treatment of non-small-cell lung cancer’ (2007). NICE Technology Appraisal 124. Guidance on static list.</p> <p>Appraisals in development:</p> <p>‘Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer’. NICE technology appraisal guidance [ID438]. Publication expected May 2015.</p> <p>‘Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175)’. NICE technology appraisal guidance [ID620]. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>‘Lung cancer: The diagnosis and treatment of lung cancer’ (2011). NICE clinical guideline 121. Review date June 2015.</p> <p>Related Quality Standards:</p> <p>‘Lung cancer for adults’ (2012). NICE quality standard</p>

	<p>17. Related NICE Pathways: <a href="#">Lung Cancer</a> (2012) NICE pathway</p>
<p><b>Related National Policy</b></p>	<p><b>National Service Frameworks</b> <a href="#">Cancer</a></p> <p><b>Department of Health</b></p> <p>Department of Health (2013) <a href="#">NHS Outcomes Framework 2014–2015</a></p> <p>Department of Health (2011) <a href="#">Improving outcomes: a strategy for cancer</a></p> <p>Department of Health (2009) <a href="#">Cancer commissioning guidance</a></p> <p>Department of Health (2007) <a href="#">Cancer reform strategy</a></p>

### Questions for consultation

- Have all relevant comparators for ramucirumab been included in the scope?
- Which treatments are considered to be established clinical practice in the NHS for locally advanced or metastatic non-small-cell lung cancer that has progressed after platinum-based chemotherapy?
- How should best supportive care be defined?

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

Where do you consider ramucirumab 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 ramucirumab 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 ramucirumab 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 ramucirumab 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

- <sup>1</sup> Cancer Research UK (2013) [Lung cancer statistics](#). Accessed March 2015.