

## National Institute for Health and Clinical Excellence

## Cetuximab for the treatment of advanced non-small cell lung cancer

## Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Cancer Network Pharmacists Forum	No issues	Comment noted
	Eli Lilly	It is appropriate	Comment noted
	Merck Serono	The opinion of Merck Serono is that it is very appropriate to refer this topic to NICE for appraisal. NSCLC is a very aggressive form of cancer with very poor prognosis. Further treatment options should be reviewed as a priority.	Comment noted
	National Lung Forum for Nurses	Yes, it should be referred for appraisal. As stated, treatment choices for patients with lung cancer are very limited at present due to late diagnosis; by which time the disease is at an advanced stage. Chemotherapy can improve symptoms but at the expense of debilitating side effects. We welcome treatments which improve the quality of life and length of life for those with lung cancer. As it is a targeted therapy, it has the potential to destroy cancer cells, whilst causing little harm to normal cells. It may increase the effectiveness of chemotherapy given.	Comment noted
	Roy Castle Lung Cancer Foundation	Yes. Patients with advanced nslc have a lack of effective treatment options available to them at the present time. It is important that this new technology is appraised.	Comment noted

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	Royal College of Nursing	There is some difficulty in making detailed comment on this as cetuximab is not yet licensed for this purpose. When it is known which indications cetuximab is licensed for (e.g. will it be first line in combination with platinum-based chemotherapy or second line in combination with single agent chemotherapy?) then it will be possible to answer questions such as what the appropriate reference treatment arm should be. It is suggested that it perhaps could be part of a multiple technology appraisal if it is going to be targeted at first line treatment along with bevacizumab.	Comment noted. The manufacturer informed consultees at the scoping workshop that it was anticipated that cetuximab would be for people who were chemotherapy naïve and that the comparator should be any platinum based chemotherapy regimen.
Wording	Cancer Network Pharmacists Forum	Objective should contain the wording “in combination with chemotherapy” to be consistent with the other documents.	Comment noted. The remit has been amended to reflect that the technology will be appraised within its licensed indication.
	Eli Lilly	Remit wording needs amending to: To appraise .... of cetuximab in the treatment of <u>previously untreated stage IIIB/IV locally advanced or metastatic</u> non-small-cell lung cancer (NSCLC).	Comment noted. The remit has been amended to reflect that the technology will be appraised within its licensed indication

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	Merck Serono	The opinion of Merck Serono is that the wording of the remit largely reflects the issues of clinical and cost effectiveness.  However, the wording should be altered to take into account the final licence when available.	Comment noted. The remit has been amended to reflect that the technology will be appraised within its licensed indication
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted
Timing Issues	Cancer Network Pharmacists Forum	No comments	Comment noted
	Eli Lilly	No comments	Comment noted
	Merck Serono	Merck Serono believes that there is high urgency for this proposed appraisal based on the poor prognosis reported for patients with NSCLC.	Comment noted
	National Lung Forum for Nurses	Appears appropriate	Comment noted
	Roy Castle Lung Cancer Foundation	Seems reasonable. Will depend on licensing schedule	Comment noted
	Royal College of Nursing	No comments	Comment noted

Section	Consultees	Comments	Action
Additional comments on the draft remit	Cancer Network Pharmacists Forum	No comments	Comment noted
	Eli Lilly	No comments	Comment noted
	Merck Serono	No comments	Comment noted
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted

**Comment 2: the draft scope**

Section	Consultees	Comments	Action
Background information	Cancer Network Pharmacists Forum	No comments	Comment noted
	Eli Lilly	No comments	Comment noted
	Merck Serono	Expert opinion provided to Merck Serono suggests the background paragraph may contain small factual inaccuracies as described below: <ul style="list-style-type: none"> <li>• The main types of NSCLC are squamous cell carcinoma (45%), adenocarcinoma (45%), and large cell carcinoma (10%).</li> <li>• Approximately 30% of patients present with local / potentially resectable disease and about 50% of these will be suitable for surgery.</li> <li>• 30% of patients present with locally and regionally advanced disease (Stage IIIb) and 40% with advanced disease (Stage IV in which there are distant metastases).</li> <li>• About one third of patients with NSCLC have disease which can be termed as “local disease”.</li> <li>• Patients who cannot tolerate a platinum combination could be termed as either elderly or poor performance status, or contraindicated.</li> </ul>	Comments noted. Amendments have been made to the background section following consultation on the scope
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	Yes – It highlights the devastating nature of this disease.	Comment noted
	Royal College of Nursing	No comments	Comment noted
The technology/ intervention	Cancer Network Pharmacists Forum	No comments	Comment noted

## Summary form

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	Eli Lilly	We presume dosage regimen will be as per license	Comment noted. The Institute appraises technologies within their licensed indications
	Merck Serono	Cetuximab treatment length of therapy is likely to be in the region of 18 weeks	Comment noted
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted
Population	Cancer Network Pharmacists Forum	No comments	Comment noted

Section	Consultees	Comments	Action
	Eli Lilly	<p>Population needs to be defined as</p> <ul style="list-style-type: none"> <li>• previously untreated</li> <li>• stage IIIB/IV NSCLC</li> <li>• Locally advanced / metastatic</li> <li>• EGFR-positive NSCLC</li> </ul> <p>The following subgroups should be considered</p> <ul style="list-style-type: none"> <li>• Poor Performance status (PS 2)</li> <li>• Smokers/non-smokers</li> <li>• Elderly patients</li> <li>• Various histological sub-groups (adenocarcinoma, squamous, non-squamous)</li> <li>• Other sub-populations (i.e., Asian females, EGFR positive)</li> </ul>	<p>Comments noted. At the scoping workshop the consultees agreed that the appraisal reference population should exclude EGFR negative patients and those who had previously been treated with chemotherapy, the population has been amended accordingly.</p> <p>At the scoping workshop the consultees explained that the prognosis may differ according to performance status (measure via EGOG) and histological class of NSCLC (carcinoma or adenoma) and tumour markers (EGFR/ FISH status). The consultees agreed that the appraisal should distinguish between these subgroups if the evidence allows. The 'other considerations' section of the scope has been amended accordingly.</p>
	Merck Serono	No comments	Comment noted

## Summary form

Section	Consultees	Comments	Action
	National Lung Forum for Nurses	As this is a targeted therapy, there may be a target group of patients more likely to respond. If so, they should be identified	Comment noted. The scope now states that, if the evidence allows, consideration will be given to subgroups such as performance status, histological class of NSCLC and tumour markers.
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted
Comparators	Cancer Network Pharmacists Forum	Due to the range of treatments available and the debate surrounding their relative efficacy, care should be taken when discussing comparators. Comparators should be relevant to UK practice.	Comment noted. Following consultation and discussions at the scoping workshop the scope has been amended to state that the comparators are combinations of platinum-based chemotherapy regimens.
	Eli Lilly	These are treatments currently used in the NHS. Best standard of care: Gemcitabine/carboplatin	Comment noted. Following consultation and discussions at the scoping workshop the scope has been amended to state that the comparators are combinations of platinum-based chemotherapy regimens.



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	Merck Serono	Treatments with a single agent is not an appropriate comparator for this appraisal and is a different population of patients who are potentially older, a lower performance status or contraindicated to platinum based treatment.	Comment noted. Following consultation and discussions at the scoping workshop the scope has been amended to state that the comparators are combinations of platinum-based chemotherapy regimens.
	National Lung Forum for Nurses	When comparing with standard treatments, important to take into account the cost of hospitalisation for iatrogenic infections as a result of chemotherapy or for symptoms associated with disease progression.	Comment noted
	Roy Castle Lung Cancer Foundation	Bevacizumab (Avastin) is likely to be licensed in advanced nsclc later this year. Will this perhaps require to be considered?	Comment noted. All standard UK clinical practice for the treatment of NSCLC will be considered as potential comparators for this appraisal.
	Royal College of Nursing	No comments	Comment noted
Outcomes	Cancer Network Pharmacists Forum	No comments	Comment noted
	Eli Lilly	Yes	Comment noted
	Merck Serono	No comments	Comment noted
	National Lung Forum for Nurses	When measuring cost effectiveness, it is important to take into account that as the survival advantage is small, the patient may need it for a matter of months rather than years.	Comment noted
	Roy Castle Lung Cancer Foundation	We would wish to underline the importance of looking at quality of life and symptom control, as well as other measures of response. These may seem relatively small benefits. However, they are very important to this patient group	Comment noted
	Royal College of Nursing	No comments	Comment noted

Section	Consultees	Comments	Action
Economic analysis	Cancer Network Pharmacists Forum	No comments	Comment noted
	Eli Lilly	No comments	Comment noted
	Merck Serono	The economic analysis is appropriate. The appropriate time horizon for assessment must take into account the average age of the intended patient population; however it would be reasonable to suggest that costs and benefits can be achieved within 5 years of treatment initiation.	Comment noted
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted
Other considerations	Cancer Network Pharmacists Forum	No comments	Comment noted
	Eli Lilly	Pemetrexed in combination with cisplatin is expected to be licensed for the first-line treatment of stage IIIB/IV locally advanced /metastatic NSCLC in 2008.	Comment noted

## Summary form

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	Merck Serono	Subgroup analyses to be potentially considered include: <ul style="list-style-type: none"> <li>• Patients with different performance status (as measured by ECOG).</li> <li>• Patients with EGFR/ FISH positive biomarker.</li> <li>• Risk share schemes.</li> </ul>	At the scoping workshop the consultees explained that the prognosis may differ according to performance status (measure via EGOG) and histological class of NSCLC (carcinoma or adenoma) and tumour markers (EGFR/ FISH status). The consultees agreed that the appraisal should distinguish between these subgroups if the evidence allows. The 'other considerations' section of the scope has been amended accordingly.
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted
Questions for consultation	Cancer Network Pharmacists Forum	Best supportive care, radiotherapy and chemo/radiotherapy are not relevant comparators.	Comment noted. Following consultation and discussions at the scoping workshop the scope has been amended to state that the comparators are combinations of platinum-based chemotherapy regimens.
	Eli Lilly	No comments	Comment noted

Section	Consultees	Comments	Action
	Merck Serono	Radiotherapy, Best Supportive care and Chemoradiotherapy are not appropriate comparators for this appraisal.	Comment noted. Following consultation and discussions at the scoping workshop the scope has been amended to state that the comparators are combinations of platinum-based chemotherapy regimens.
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted
Additional comments on the draft scope.	Cancer Network Pharmacists Forum	No comments	Comment noted
	Eli Lilly	No comments	Comment noted
	Merck Serono	No comments	Comment noted
	National Lung Forum for Nurses	No comments	Comment noted
	Roy Castle Lung Cancer Foundation	No comments	Comment noted
	Royal College of Nursing	No comments	Comment noted

**Comment 4: Regulatory issues**

<b>Section</b>	<b>Consultees</b>	<b>Comments</b>	<b>Action</b>
Remit	Merck Serono	No comments	Comment noted
Current or proposed marketing authorisation	Merck Serono	No comments	Comment noted

**The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope**

Breathe Easy Colchester  
 British Thoracic Society  
 Marie Curie Cancer Care  
 NHS QIS  
 Royal College of Pathologists  
 Royal Pharmaceutical Society  
 Department of Health (DOH)  
 Macmillan Cancer Support