NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Gefitinib for the first-line treatment of locally advanced or metastatic non-small cell lung cancer

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Roy Castle Lung Cancer Foundation	No comments.	Comment noted
	RCN	This seems accurate.	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	Accurate and complete.	Comment noted
	AstraZeneca	No comments.	Comment noted
The technology/ intervention	Roy Castle Lung Cancer Foundation	Oral, easy to administer. Relatively low toxicity.	Comment noted
	RCN	This seems accurate.	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	Yes.	Comment noted

Section	Consultees	Comments	Action
	AstraZeneca	Gefitinib is a potent and selective inhibitor of the epidermal growth factor receptor (EGFR) tyrosine kinase. Activation of the tyrosine kinase catalyses autophosphorylation and subsequent phosphorylation of protein tyrosine residues, which then initiates a cellular signal transduction cascade. Selective inhibition of the EGFR tyrosine kinase with gefitinib results in interruption of mitogenic and anti-apoptotic signals responsible for cellular cancer processes such as proliferation, growth, metastases, angiogenesis and responsiveness to chemotherapy or radiotherapy. There is now considerable evidence of expression and over-expression of EGFR in an extensive range of human cancers eg, non-small cell lung cancer (NSCLC) as well as prostate, colorectal, head and neck, bladder, breast and gastric cancers. Importantly, over-expression of EGFR has been correlated with poor prognosis features in many cases. In recent studies the efficacy of gefitinib has been clearly correlated to the mutation status for the EGFR gene with EGFR mutation positive patients benefiting most from gefitinib treatment."	Comment noted. Technologies are appraised within their licensed indications.
Population	Roy Castle Lung Cancer Foundation	Anyone with a lung cancer diagnosis? What about those who have already received first line and / or second line therapy and are mutation positive?	Following the scoping workshop, consultees agreed that the population section of the scope should be updated to state: 'People with previously untreated EGFR-TK mutation positive locally advanced or metastatic NSCLC'.
	RCN	This has been defined appropriately.	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	No comments.	Comment noted

Section	Consultees	Comments	Action
	AstraZeneca	For the first line treatment of adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating mutations of EGFR-TK.	Following the scoping workshop, consultees agreed that the population section of the scope should be updated to state: 'People with previously untreated EGFR-TK mutation positive locally advanced or metastatic NSCLC'.
Comparators	Roy Castle Lung Cancer Foundation	Not entirely sure that the appropriate comparator is standard first line chemotherapy or Pemetrexed. What about response when given to EGFR-TK mutation positive patients and to mutation negative patients?	Comment noted. Consultees at the scoping workshop agreed that platinum based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine may be used in some patients in UK clinical practice and should remain as a comparator in the scope. Consultees also agreed that pemetrexed should remain as a comparator in the scope as it licensed for first line treatment of NSCLC and pemetrexed is currently being appraised within its licensed indication by NICE.
	RCN	These are the standard treatments routinely used in clinical practice.	Comment noted

Section	Consultees	Comments	Action
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	These patients would normally be offered palliative chemotherapy if of adequate performance status – there are other factors that determine the use of chemotherapy such as age, renal function and patient preference. Alternatives would include best supportive care, or palliative radiotherapy. Pemetrexed is not currently used as first line treatment in the UK and when it is likely to be used in combination with a platinum-based drug.	Comment noted. Following the scoping workshop, consultees agreed that the comparators section of the scope should state: Platinum based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine; Pemetrexed in combination with platinum based chemotherapy (carboplatin or cisplatin); and best supportive care.
	AstraZeneca	AstraZeneca does not believe pemetrexed in combination with cisplatin to be a standard treatment currently in use within the NHS. AstraZeneca believes that the comparators stated in the draft scope do not represent routine UK clinical practice. From market research and a study looking at chemotherapy usage in the first line setting, platinum-based chemotherapy in combination with vinorelbine only represented ~12% of all first line chemotherapy use. AstraZeneca would like to query whether this represents routine UK clinical practice.	Comment noted. Consultees agreed that pemetrexed should remain as a comparator in the scope since it licensed for first line treatment of NSCLC and pemetrexed is currently being appraised within its licensed indication by NICE. Consultees at the scoping workshop agreed that platinum based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine may be used in some patients in UK clinical practice and should remain as a comparator in the scope.

Section	Consultees	Comments	Action
Outcomes	Roy Castle Lung Cancer Foundation	Note, that the prognosis for this patient group is very poor and relatively small benefits would be of significant importance to patients.	Comment noted
	RCN	Yes	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	Yes	Comment noted
	AstraZeneca	The outcome measures listed in the draft scope do capture the most important health-related benefits of gefitinib.	Comment noted
Economic analysis	Roy Castle Lung Cancer Foundation	No comments.	Comment noted
	RCN	No comments.	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	No comments.	Comment noted

Section	Consultees	Comments	Action
	AstraZeneca	Platinum-based doublet chemotherapy is recommended as the 1st line treatment for NSCLC. Since EGFR testing is not required for current treatment of NSCLC the base case economic analysis should evaluate the cost-effectiveness of gefitinib in EGFR M+ vs. doublet chemotherapy in an untested population. Time horizon - a time horizon of 6 years will be adopted for the cost-effectiveness analysis. This is consistent with the poor prognosis of patients diagnosed with lung cancer, with fewer than 5% surviving beyond 5 years. It is also consistent with the time horizon adopted in the pemetrexed 1st line STA submission.	Comment noted
Equality and Diversity	Roy Castle Lung Cancer Foundation	No comments.	Comment noted
	RCN	No comments.	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	No comments.	Comment noted
	AstraZeneca	No comments.	Comment noted
Other considerations	Roy Castle Lung Cancer Foundation	In recent years, there has been a suggestion that those most likely to respond are 'female, non-smokers, with adenocarcinoma and of oriental origin'. Assessment of these characteristics may be helpful.	Comment noted. The 'Other considerations' section of the scope states that 'If evidence allows the following subgroups will be considered: performance status, histology, gender, and previous smoking history'.
	RCN	No comments.	Comment noted

Section	Consultees	Comments	Action
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	These patients would normally be offered palliative chemotherapy if of adequate performance status – there are other factors that determine the use of chemotherapy such as age, renal function and patient preference. It will be important to consider that use of an active oral drug that has significantly less toxicity than standard intravenous chemotherapy, may allow many more patients to be treated than are currently. A simple direct comparison with standard chemotherapy might not take this into account.	Comment noted. Comment noted. Following the scoping workshop, consultees agreed that the comparators section of the scope should state: Platinum based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine; Pemetrexed in combination with platinum based chemotherapy (carboplatin or cisplatin); and best supportive care.
	AstraZeneca	On the basis of the available data, AstraZeneca believes that mutation status is driving the benefit in all other clinically defined sub-groups as well as biomarker sub-groups and therefore AstraZeneca believes that any treatment decision based on subgroups other than EGFR mutation status is not appropriate.	Comment noted. Following the scoping workshop consultees agreed that performance status, histology, gender, and previous smoking history should remain in the scope as subgroups to be considered if evidence allows.
Questions for consultation	Roy Castle Lung Cancer Foundation	No comments.	Comment noted
	RCN	No comments.	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	No comments.	Comment noted
	AstraZeneca	No comments.	Comment noted

Section	Consultees	Comments	Action
Additional comments on the draft scope.	Roy Castle Lung Cancer Foundation	It is unfortunate that, with short notice, we are unable to attend the Scoping Meeting on 22nd July 2009. The licensing of this product in lung cancer and its effect on pathology services, will require changes. Its place in the management of NSCLC, would perhaps be best considered by the NICE Guideline Development Group (currently part updating the 2005 Lung Cancer Guideline) – we hope that this Appraisal will take in to account the opinions of this multidisciplinary group. The drug is proposed for use only in EGFR-TK positive tumours. This is not currently a routine histopathological test and organisations would need to bring this into routine care. Many patients with stage IIIB/IV lung cancer will be diagnosed on cytological as opposed to histopathological specimens. It is feasible to ascertain the EGFR status on small cytology specimens – if not then either the drug will be denied to suitable patients, or alternatively diagnostic pathways will need to be altered, potentially exposing patients to more invasive tests in an era where minimal access and small samples are considered good practice.	Comment noted. Consideration will be given to related NICE guidance such as clinical guidelines. Please the 'Related NICE guidance' section of the scope. Comment noted. Comment noted
	RCN	No comments.	Comment noted
	British Thoracic Society Lung Cancer and Mesothelioma Specialist Advisory Group	No comments.	Comment noted
	AstraZeneca	No comments.	Comment noted

Comment 4: Regulatory issues

Section	Consultees	Comments	Action
Remit	AstraZeneca	N/A	Comment noted
Current or proposed marketing authorisation	AstraZeneca	*What are the current indications for the technology?* Not currently licensed in the UK *What are the planned indications for the technology?* IRESSA is indicated for the treatment of adult patients with locally advanced or metastatic non small cell lung cancer (NSCLC) with activating mutations of EGFR TK. *What is the target date (mm/yyyy) for regulatory submission?* N/A *Which regulatory process are you following?* Centralised process *What is the anticipated date (mm/yyyy) of CHMP positive opinion (if applicable) and regulatory approval?* COMMERCIAL IN CONFIDENCE DATA HAS BEEN REMOVED	Comment noted Comment noted Comment noted Comment noted

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

Welsh Assembly Government
Royal Pharmaceutical Society
RICE – The Research Institute for the Care of Older People
NHS QIS
Macmillan Cancer Support
Department of Health
British Thoracic Oncology Group
Eli Lilly