NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Nintedanib for previously treated locally advanced, metastatic or locally recurrent non-small cell lung cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of nintedanib within its licensed indication for previously treated locally advanced, metastatic or locally recurrent non-small cell lung cancer of adenocarcinoma tumour histology[1].

Background

Lung cancer falls into 2 main histological categories: around 85-90% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers. Non-small cell lung cancer (NSCLC) can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma. The majority of lung cancers are diagnosed in the later stages of the disease, with 21% presenting with locally and regionally advanced disease (stage IIIB) and 48% presenting with advanced disease (stage IV) in which the cancer has spread to other parts of the body. For people presenting with NSCLC stage IIIB the 5-year survival rate is around 7 to 9%; for people presenting with NSCLC stage IV the 5-year survival rate varies from 2 to 13%. In England and Wales there were 35,406 people newly diagnosed with lung cancer and 29,914 deaths registered in 2010.

While one-third of people with NSCLC have disease which is suitable for potentially curative surgical resection, for the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. NICE clinical guideline 121 (CG121) recommends a combination of docetaxel, gemcitabine, paclitaxel or vinorelbine plus carboplatin or cisplatin as first-line treatment options for patients with stage III or IV NSCLC and a good performance status. People who are unable to tolerate a platinum combination may be offered single-agent chemotherapy. NICE technology appraisal guidance 192 and 258 recommend gefitinib (TA192) and erlotinib (TA258) as options for the first-line treatment of people with locally advanced or metastatic NSCLC if they test positive for the EGFR-tyrosine kinase mutation. NICE technology appraisal guidance 181 recommends pemetrexed in combination with cisplatin as an option for the first-line treatment of locally advanced or metastatic NSCLC if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma. NICE technology appraisal guidance 190 recommends pemetrexed as an option for the maintenance treatment of

[1] The remit and scope were update in line with the wording of the therapeutic indication in the positive CHMP opinion.

people with locally advanced or metastatic NSCLC other than predominantly squamous cell histology if the disease has not progressed immediately following platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel. For people with locally advanced or metastatic NSCLC whose disease has progressed following prior chemotherapy, NICE clinical guideline 121 recommends docetaxel monotherapy if second-line therapy is considered appropriate. NICE technology appraisal 162 (currently being reviewed) also recommends erlotinib as another second-line treatment option for NSCLC. Best supportive care is considered for some people whose performance status means that they are unlikely to tolerate chemotherapy.

The technology

Nintedanib (brand name unknown, Boehringer Ingelheim) is an inhibitor of the vascular endothelial growth factor receptor, the platelet-derived growth factor receptor and the fibroblast growth factor receptor. All 3 growth factors are involved in tumour vascularisation and inhibition of them may play a role in the prevention of tumour growth and spread. It is administered orally.

Nintedanib does not currently have a UK marketing authorisation for previously treated NSCLC but has received a positive CHMP opinion on 25th September 2014 in combination with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after first-line chemotherapy'. It has been studied in combination with docetaxel in adults with stage IIIB/IV or recurrent NSCLC which has progressed following first-line chemotherapy, compared with placebo plus docetaxel. It has also been studied in combination with pemetrexed in adults with stage IIIB/IV or recurrent non-squamous NSCLC which has progressed following first-line chemotherapy, compared with placebo plus pemetrexed.

Intervention(s)	Nintedanib in combination with docetaxel
Population(s)	Adults with locally advanced, metastatic or locally recurrent non-small cell lung cancer of adenocarcinoma tumour histology
Comparators	• docetaxel monotherapy • erlotinib
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rates • 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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE pathways	Related Technology Appraisals: Technology Appraisal No. 162, Nov 2008, 'Erlotinib for the treatment of non-small cell lung cancer'. Currently being reviewed with TA175. Technology Appraisal No. 124, Nov 2007, 'Pemetrexed for the treatment of non-small-cell lung cancer'. Guidance on static list. Terminated Technology Appraisal No. 175, Jul 2009, 'Gefitinib for the second-line treatment of locally advanced or metastatic non-small cell lung cancer.' Currently being reviewed with TA162. Technology Appraisal in preparation, 'Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175)'. Expected date of publication tbc. Related Guidelines: Clinical Guideline No. 121, Apr 2011, 'The diagnosis and treatment of lung cancer' (replaces NICE clinical guideline 24). Related Quality Standards: Quality Standard No. 17, Mar 2012, 'Lung cancer for adults'. Related NICE Pathways: NICE Pathway: Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer
Related national policy	NHS England (2013) Manual for prescribed specialised services (Chapter 18) http://www.england.nhs.uk/wp-

	content/uploads/2014/01/pss-manual.pdf Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy