

# National Horizon Scanning Centre

## Sorafenib (Nexavar) for advanced non-small cell lung cancer

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This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

## Sorafenib (Nexavar) for advanced non-small cell lung cancer

### Target group

- Non-small cell lung cancer (NSCLC) - stages IIIb and IV, chemotherapy naïve.

### Technology description

Sorafenib (BAY 43-9006, Nexavar) is the lead compound in a series of raf signalling pathway inhibitors with raf kinase inhibitor activity. It has a dual action that targets serine/threonine and receptor tyrosine kinases, inhibiting (1) the raf cascade to prevent the downstream mediation of cell growth and proliferation, and (2) the VEGFR-2,3/PDGFR- $\beta^a$  signalling cascade to inhibit the activation of angiogenesis, thus acting on both tumour cell growth and tumour vasculature. Sorafenib is an oral treatment taken at 400mg twice daily.

Sorafenib is licensed for:

- Advanced renal cell carcinoma in patients who have failed or are unsuitable for interleukin-2 or interferon-alpha based therapy.
- Hepatocellular carcinoma.

Sorafenib is in phase III development for malignant melanoma and in phase II development for advanced breast cancer.

### Innovation and/or advantages

Sorafenib could provide a new treatment option and may increase survival in NSCLC.

### Developer

Bayer AG; Onyx Pharmaceuticals

### Place of use

- |  |   |  |
|--|---|--|
| <input type="checkbox"/> Home care e.g. home dialysis                                    | <input type="checkbox"/> Community or residential care e.g. district nurses, physio | <input type="checkbox"/> Primary care e.g. used by GPs or practice nurses    |
| <input checked="" type="checkbox"/> Secondary care e.g. general, non-specialist hospital | <input type="checkbox"/> Tertiary care e.g. highly specialist services or hospital  | <input type="checkbox"/> Emergency care e.g. paramedic services, trauma care |
| <input type="checkbox"/> General public e.g. over the counter                            | <input type="checkbox"/> Other:   |  |

### NHS or Government priority area:

This topic is relevant to the NHS Cancer Plan.

### Relevant guidance

#### NICE clinical guideline

- Lung Cancer: the diagnosis and treatment of lung cancer. 2005 (expected review date February 2009)<sup>1</sup>.

#### NICE technology appraisals

- Pemetrexed for the treatment of non-small cell lung cancer. 2007<sup>2</sup>.
- Docetaxel, paclitaxel, gemcitabine and vinorelbine for the treatment of non-small cell lung cancer. 2001 (now replaced by NICE Clinical Guideline on Lung Cancer, 2005)<sup>3</sup>.
- Bevacizumab for non-small cell lung cancer. Expected January 2008<sup>4</sup>.

<sup>a</sup> VEGFR: vascular endothelial growth factor receptor; PDGFR: platelet-derived growth factor receptor.

- Erlotinib for advanced non-small cell lung cancer. Expected April 2008<sup>5</sup>.

#### Other guidance

- Scottish Intercollegiate Guidelines Network (SIGN): Management of patients with lung cancer. 2005<sup>6</sup>.
- European Society for Medical Oncology (ESMO): Minimum clinical recommendations for the diagnosis, treatment and follow-up of non-small cell lung cancer. 2005<sup>7</sup>.
- US National Comprehensive Cancer Network (NCCN): clinical practice guideline on non-small cell lung cancer. 2007<sup>8</sup>.

### **Clinical need and burden of disease**

Lung cancer is the most common cause of cancer-related death in both men and women. There were 32,715 new cases of lung cancer in England and Wales in 2004 (an incidence of around 68 cases per 100,000 population) and 28,632 deaths registered in 2005 (a rate of around 54 deaths per 100,000 population)<sup>9</sup>. In England and Wales lung cancer has a one-year survival rate of 25% and a five-year survival rate of 7%<sup>10</sup>.

NSCLC accounts for approximately 80% of all lung cancers. Approximately 75% of newly diagnosed patients already have advanced (stage III or IV) disease<sup>11</sup> (equating to around 24,536 patients in England and Wales), with a five-year survival rate of less than 1%<sup>12</sup>. NICE estimates that around 25% of patients with advanced nsclc receive first-line chemotherapy<sup>13</sup>.

### **Existing comparators and treatments**

Treatment options for stage IIIB or IV NSCLC include radiation therapy, chemotherapy plus radiation therapy, and chemotherapy alone. Chemotherapy may be recommended for patients with non-resectable stage III or IV disease provided they have a good performance status. Current NICE guidance recommends that first-line chemotherapy should include a combination of a platinum drug (cisplatin or carboplatin) and a single third generation drug, such as docetaxel, gemcitabine, paclitaxel or vinorelbine.

### **Efficacy and safety**

Trial name or code	Trial ID: 12006; phase III <sup>14</sup>	Trial ID: 11961; Phase III <sup>15</sup>	Phase II <sup>16,17,18</sup>
Sponsor	Bayer HealthCare AG.	Bayer HealthCare AG.	Bayer Healthcare AG.
Status	Ongoing (began Q1 2007).	Ongoing (began Q1 2006)	Abstract
Location	Europe (inc UK); Israel; China; Mexico.	USA; Europe (inc. UK); Russia; Asia; South America; Australia; Canada.	USA; EU
Design	Randomised; double blind; placebo control.	Randomised; double-blind.	Non-randomised; open label; uncontrolled.
Participants in trial	n=350; stage IIIB (with pericardial or pleural effusion) or stage IV NSCLC squamous or non-squamous chemotherapy naïve; ECOG performance status 0 or 1. Randomised to: <b>Arm 1:</b> gemcitabine 1250 mg/m <sup>2</sup> iv, cisplatin 75 mg/m <sup>2</sup> iv, and sorafenib 400 mg twice daily; or	n=900; stage IIIB or stage IV nsclc; chemotherapy naïve; ECOG performance status of 0 or 1.	n=52; refractory stage IV nsclc.  Sorafenib 400mg twice daily over 28 day cycles. Continuous treatment for maximum of 2 years.

	<b>Arm 2:</b> Gemcitabine 1250 mg/m <sup>2</sup> iv, cisplatin 75 mg/m <sup>2</sup> iv, and placebo.		
Follow-up	Until primary endpoint and clinical benefit.	Until primary endpoint and clinical benefit	-
Primary outcome	Progression free survival (PFS).	Overall survival (OS)	QOL; PFS; OS; biomarkers; safety.
Secondary outcomes	Quality of life (QOL); biomarkers; safety.	PFS; response; duration of response; QOL; safety.	QOL; response; health economics.
Key results	-	-	Median PFS for stable disease (n=30) 23.7 weeks. Median PFS for all patients 11.9 weeks, median overall survival 29.3 weeks. QOL: Mean total FACT-L <sup>b</sup> scores 99.3, 106.5 and 83.7 at cycles 2, 4 and end of treatment, respectively. Mean changes in total FACT-L score: -4.6, -0.2, and -14.6.
Adverse effects	-	-	Most frequent adverse effects: diarrhoea; hand-foot skin reaction; fatigue; nausea

### Estimated cost and cost impact

The cost of sorafenib at a dose of 2 x 200 mg tablets twice daily for 28 days is around £2,504<sup>c</sup>.

### Potential or intended impact – speculative

#### Patients

- |   |   |   |
|---|---|---|
| <input type="checkbox"/> Reduced morbidity  | <input checked="" type="checkbox"/> Reduced mortality or increased survival | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker, earlier or more accurate diagnosis or identification of disease | <input type="checkbox"/> Other:   | <input type="checkbox"/> Non identified   |

#### Services

- |  |  |   |
|--|--|---|
| <input type="checkbox"/> Increased use | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input type="checkbox"/> Decreased use | <input type="checkbox"/> Other:                          | <input checked="" type="checkbox"/> Non identified  |

#### Costs

- |  |  |   |
|--|--|---|
| <input type="checkbox"/> Increased unit cost compared to alternative | <input type="checkbox"/> Increased costs: more patients coming for treatment | <input type="checkbox"/> Increased costs: capital investment needed |
| <input checked="" type="checkbox"/> New costs: additional therapy    | <input type="checkbox"/> Savings:  | <input type="checkbox"/> Other:                                     |

<sup>b</sup> FACT-L: Functional assessment of cancer therapy - lung

<sup>c</sup> Costs taken from British National Formulary, number 54. September 2007

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