

## National Horizon Scanning Centre

# Pemetrexed disodium (Alimta) monotherapy as maintenance therapy for 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.

## **Pemetrexed disodium (Alimta) monotherapy as maintenance therapy for non-small cell lung cancer**

### **Target group**

- Non-small cell lung cancer (NSCLC), other than predominantly squamous cell histology, stage IIIB or IV: maintenance therapy after first-line induction therapy of four cycles of platinum-based chemotherapy.

### **Technology description**

Pemetrexed disodium (Alimta, LY231514) is a folic acid analogue. It inhibits enzymes in the folate pathway essential for cell replication including: thymidylate synthase, dihydrofolate reductase and glycinamide ribonucleotide formyltransferase (GARFT). Pemetrexed disodium 500mg/m<sup>2</sup> is administered as a 10-minute intravenous (IV) infusion every 21 days (along with vitamin B12 and folate supplementation and a corticosteroid). Pemetrexed is intended as a maintenance therapy for patients whose cancer has not progressed during standard platinum-based induction chemotherapy.

Pemetrexed disodium is licensed in the EU for:

- NSCLC - other than predominantly squamous cell histology, locally advanced or metastatic disease, first-line treatment, in combination with cisplatin.
- NSCLC - other than predominantly squamous histology locally advanced or metastatic, after prior chemotherapy.
- Malignant pleural mesothelioma - chemotherapy naïve patients, in combination with cisplatin.

Pemetrexed disodium in combination with cisplatin is currently in phase III trials for recurrent or metastatic head and neck cancer.

### **Innovation and/or advantages**

Pemetrexed is the first maintenance chemotherapy for NSCLC targeted at non-squamous histology.

### **Developer**

Eli Lilly.

### **Availability, launch or marketing dates, and licensing plans:**

In phase III clinical trials.

### **NHS or Government priority area:**

This topic is relevant to the NHS Cancer Plan (2000).

### **Relevant guidance**

#### NICE technology appraisals

- NICE 18<sup>th</sup> work programme: technology appraisal minded referrals in March 2008<sup>1</sup>.
- NICE technology appraisal. Pemetrexed for the treatment of malignant pleural mesothelioma. 2008<sup>2</sup>.
- NICE technology appraisal. Pemetrexed for the treatment of non-small cell lung cancer. 2007<sup>3</sup>.
- NICE technology appraisal in development. Bevacizumab for the treatment of non-small cell lung cancer. Suspended until further notice<sup>4</sup>.

- NICE technology appraisal in development. Cetuximab for the treatment of advanced non-small cell lung cancer. Issue date to be confirmed<sup>5</sup>.
- NICE technology appraisal in development. Erlotinib for the treatment of advanced non-small cell lung cancer. Expected date of issue June 2008<sup>6</sup>.
- NICE technology appraisal in development. Gefitinib for the treatment of non-small cell lung cancer. Expected date of issue November 2009<sup>7</sup>.

#### NICE clinical guidelines

- NICE clinical guideline in development. Diagnosis and management of metastatic malignant disease of unknown primary origin. Expected date of issue 2010<sup>8</sup>.
- NICE clinical guideline. Lung Cancer: the diagnosis and treatment of lung cancer. 2005<sup>9</sup>.
- Scottish intercollegiate guidelines network. Management of patients with lung cancer. 2005<sup>10</sup>.

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

Lung cancer is the leading cause of cancer-related mortality in both men and women. There were 32,715 new cases of lung cancer in England and Wales in 2004 and 28,632 deaths in 2005. In England and Wales lung cancer has a one-year survival rate of around 25% and a five-year survival rate of around 7%. NSCLC accounts for approximately 80% of all lung cancers, with the main types being squamous cell carcinoma (35%), adenocarcinoma (27%) and large cell carcinoma (10%)<sup>8</sup>. More than two-thirds of lung cancers are diagnosed at a late stage when curative treatment is not possible<sup>11</sup>.

Evidence relating to the number of patients receiving chemotherapy in England and Wales is scarce and contradictory. When estimating the cost impact of its 2005 guidance on the treatment of lung cancer, NICE used an upper estimate of 30% as the proportion of patients with advanced NSCLC who might potentially receive chemotherapy<sup>12</sup> (an estimated 5,742 patients).

#### **Existing comparators and treatments**

Maintenance therapy is currently not part of standard care.

Induction chemotherapy is recommended for some patients with non-resectable stage III or IV provided they have a good performance status (PS) (0 or 1 on the World Health Organisation performance status scale, or a Karnofsky score of 80-100):

- Combination of a single third-generation drug (gemcitabine, docetaxel, paclitaxel or vinorelbine) with a platinum drug (carboplatin or cisplatin).

#### **Efficacy and safety**

Trial code	NCT00102804 <sup>13</sup> . Pemetrexed versus placebo; Phase III.
Sponsor	Eli Lilly
Status	Complete, abstract published <sup>14</sup> .
Location	Worldwide
Design	Randomised, double-blind, placebo control.
Participants in trial	n=663; adults; stage IIIB/IV NSCLC; no progression after 4 cycles of platinum-based induction chemotherapy (docetaxel or gemcitabine or paclitaxel, in combination with a platinum). Randomised to: Pemetrexed 500mg/m <sup>2</sup> or placebo on day 1 and every 21 days until disease progression.

Follow-up	To measured progressive disease.
Primary outcome	Progression free survival (PFS).
Secondary outcomes	Overall survival time (OS); time to objective progressive disease; time to worsening of symptoms; tumour response; adverse events; symptom scores and quality of life using the lung cancer symptoms scale (LCSS).
Key results	Overall NSCLC population (based on 55% censored data): PFS median pemetrexed vs. placebo 4.3 vs. 2.6 months respectively (Hazard ratio [HR] 0.502, 95% CI: 0.42-0.61 p<0.00001); OS (median) pemetrexed vs. placebo 13.0 vs. 10.2 months respectively (HR 0.798, 95% CI 0.63-1.01, p=0.060). Histological subgroups (based on 55% censored data): Overall survival (incremental benefit, median): All non-squamous: 5.0 months; adeno carcinoma 4.7 months; large cell 3.6 months; other 4.3 months.
Expected reporting date	Final data February 2009
Adverse effects	Grade 3-4 anaemia (pemetrexed 4.5% vs. placebo 1.4%); total serious adverse events (SAEs) pemetrexed 4.3% vs. placebo 0%.

### Estimated cost and cost impact

Assuming a body surface area of 1.7m<sup>2</sup> and dose per cycle of 850mg. Pemetrexed maintenance therapy would cost £1,440 per cycle. Additional costs associated with pemetrexed administration are vitamin supplementation (folic acid and vitamin B12) and pre-treatment with dexamethasone at approximately £17 per cycle.

### 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"/> None identified  |

#### Services

- |   |  |   |
|---|--|---|
| <input checked="" type="checkbox"/> Increased use: IV administration. | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input type="checkbox"/> Decreased use                                | <input type="checkbox"/> Other:                          | <input type="checkbox"/> None 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 costs.     | <input type="checkbox"/> Savings:  | <input type="checkbox"/> Other:                                     |

### References

<sup>1</sup> Department of Health. NICE 18th work programme: technology appraisal minded referrals in March 2008. Available at:

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_083774](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_083774) (Accessed 22/04/08).

<sup>2</sup> National Institute for Clinical Excellence. Pemetrexed for the treatment of malignant pleural mesothelioma. Technology appraisal 135. January 2008.

<sup>3</sup> National Institute for Health and Clinical Excellence, Pemetrexed for the treatment of non-small cell lung cancer, NICE Guidance 124, August 2007, London: NICE

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- <sup>4</sup> National Institute for Clinical Excellence. Bevacizumab for the treatment of non-small cell lung cancer. Technology appraisal in progress. Suspended until further notice.
- <sup>5</sup> National Institute for Clinical Excellence. Cetuximab for the treatment of advanced non-small cell lung cancer. Technology appraisal in progress. Issue date to be confirmed.
- <sup>6</sup> National Institute for Clinical Excellence. Erlotinib for the treatment of advanced non-small cell lung cancer. Technology appraisal in progress. Expected date of issue June 2008.
- <sup>7</sup> National Institute for Clinical Excellence. Gefitinib for the treatment of non-small cell lung cancer. Technology appraisal in progress. Expected date of issue November 2009.
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- <sup>10</sup> Scottish Intercollegiate Guidelines Network, Management of Patients with Lung Cancer, Guideline 80, February 2005, Edinburgh: SIGN
- <sup>11</sup> Cancer Research UK. Lung cancer. Available at: <http://info.cancerresearchuk.org/cancerstats/types/lung/incidence/> (Accessed 21/04/08).
- <sup>12</sup> National Institute for Clinical Excellence, Lung cancer: The diagnosis and treatment of lung cancer, National cost-impact report, February 2005.
- <sup>13</sup> Clinical trials. NCT00102804. A phase 3, double-blind, placebo-controlled study of maintenance pemetrexed plus best supportive care versus best supportive care immediately following induction treatment for advanced non-small cell lung cancer. Available at: <http://clinicaltrials.gov/show/NCT00102804> (Accessed 21/04/08).
- <sup>14</sup> Ciuleanu T, Brodowicz T, Belani C et al. Maintenance pemetrexed plus best supportive care (BSC) versus placebo plus BSC: a phase III study. *Journal of Clinical Oncology* 2008; 26.

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