NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Topotecan for the second-line treatment of small cell lung cancer

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of topotecan within its licensed indication for the second-line treatment of small cell lung cancer.

Background

Small cell lung cancer (SCLC) is a type of lung cancer which grows rapidly and spreads quickly to distant sites. Common symptoms of SCLC include weight loss, malaise, bone pain, breathlessness and haemoptysis. SCLC is frequently associated with distinct paraneoplastic syndromes which are not due to direct invasion of adjacent tissues by the cancer or its metastases, for example, neurological or endocrine syndromes.

Lung cancer accounts for around 33,000 deaths per year in England and Wales. It is estimated that SCLC constitutes about 10% of the total cases representing about 3,300 new cases per year. Of these, around 24% are classed as limited stage at diagnosis (tumour confined to one side of the chest or to the neck lymph nodes), while the remainder have extensive stage disease (defined as the presence of obvious metastatic disease). The proportion of lung cancer cases of small cell type has been steadily falling over the years and reasons for this are unclear, but it has been attributed to changing smoking habits and a reduction in the tar content of cigarettes.

The prognosis of SCLC is poor; the life expectancy of those with untreated SCLC is about 3.5 months for limited disease and 6 weeks for extensive disease. Prognosis has been linked to performance status and extent of disease, among other factors.

Current management usually consists of combination chemotherapy regimens. Median survival with such cytotoxic treatment is approximately 14 to 18 months for limited disease and 9 to 12 months for extensive disease. Radiotherapy may be given concurrently with chemotherapy or as part of palliative care. Surgery is only suitable for a small minority of patients with no evidence of local spread or metastasis.

The NICE lung cancer clinical guideline (No. 24) advises that:

- All patients with newly diagnosed SCLC should be offered a platinum-based chemotherapy, and multi-drug regimes.
- Patients with limited-stage SCLC should be offered thoracic irradiation concurrently with the first or second cycle of chemotherapy, or

following completion of chemotherapy if there has been at least a good partial response within the thorax.

- For patients with extensive disease, thoracic irradiation should be considered following chemotherapy if there has been a complete response at distant sites and at least a good partial response within the thorax.
- Second-line chemotherapy should be offered to patients at relapse only if their disease responded to first-line chemotherapy.

The technology

Topotecan (Hycamtin, GlaxoSmithKline) acts by inhibiting topoisomerase I, an enzyme that is required for DNA replication, leading to cell death. It can be administered either orally or intravenously. Topotecan is indicated as monotherapy for patients with relapsed small cell lung cancer [SCLC] for whom re-treatment with the first-line regimen is not considered appropriate.

Intervention	• Oral topotecan • Intravenous topotecan
Population(s)	Adults with relapsed small cell lung cancer (SCLC) for whom re-treatment with the first line regimen is not considered appropriate.
Standard comparators	• Oral and intravenous topotecan will be compared with each other • Best/Active supportive care (including radiotherapy) • CAV (cyclophosphamide, doxorubicin, vincristine) • Other chemotherapy regimens
Outcomes	The outcome measures to be considered include: • time to progression • progression free survival • response rate • response duration • overall survival • symptom control • 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. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Effectiveness data for oral and intravenous topotecan should not be combined. If evidence allows subgroups of patient populations in whom the technology is clinically effective and cost effective should be considered. These may include subgroups by whether there are liver metastases, whether there are cardiovascular contraindications to anthracycline use, and by time to relapse.
Related NICE recommendations	Related NICE clinical guideline: Clinical Guideline No. 24, February 2005, 'Lung cancer: the diagnosis and treatment of lung cancer', [review expected, February 2009].