NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Pemetrexed disodium for the treatment of malignant pleural mesothelioma

Draft scope

Appraisal objective

To appraise the clinical and cost effectiveness of pemetrexed disodium (Alimta, Eli Lilly) for the treatment of malignant pleural mesothelioma, and to provide guidance to the NHS in England and Wales1,2.

Background

Malignant mesothelioma is a type of cancer which occurs in the mesothelium, a membranous lining which surrounds most internal organs. The mesothelium surrounding the lungs is known as the pleura and the mesothelium in the abdominal cavity is called the peritoneum. Cancers which occur in these lining tissues are named pleural mesothelioma and peritoneal mesothelioma respectively. Over 90% of mesothelioma with a known first site occurs as pleural mesothelioma.

Median survival from diagnosis varies from study to study within a range of 8 to 14 months.

Over 99% of deaths caused by mesothelioma have been linked to asbestos exposure. When asbestos fibres are inhaled or swallowed, they cause scarring of the lung tissues and sometimes cancers in the pleura and peritoneum. Cases of mesothelioma occur in people who have worked in the building and manufacturing industries using asbestos or used asbestos products, particularly in construction and engineering. Family members of people exposed to asbestos also have a higher risk of developing mesothelioma. The use of all asbestos was banned in 1999 in the UK.

Mesothelioma does not usually develop until 10-60 years after exposure to asbestos, the median time being of the order of 40 years. Currently, about 1700 people in the UK are diagnosed with mesothelioma each year. It is estimated that the number of people diagnosed with mesothelioma each year will increase to a peak of over 2000 cases each year between years 2015 and 2020, reflecting a lag from the highest use of asbestos in the 1970s.

Surgery is indicated for a small proportion of patients (some 1 to 5%) whose disease is at Stage I or occasionally Stage II using the Butchart

[1]The Department of Health and Welsh Assembly government remit to the Institute: To appraise the clinical and cost effectiveness of pemetrexed disodium for mesothelioma.
[2]Because pemetrexed disodium is licensed only for malignant pleural mesothelioma, the appraisal objective has been amended accordingly.

staging system. Such patients have a much longer survival rate (15% at 5 years) than patients unsuitable for surgery. For people whose disease has spread, treatments include draining the pleural cavity of excess fluid and applying a talc poudrage, radiotherapy either as prophylaxis (following drainage or biopsy) or as palliation of pain or reducing chest wall masses, and chemotherapy.

There appears to be no standard chemotherapy treatment for mesothelioma. Many different combinations of drugs are used, though none is licensed for this indication other than the drug combination under consideration in this appraisal. Agents which have consistently been reported to produce response rates of 10–20% include doxorubicin, epirubicin, mitomycin, cyclophosphamide, ifosfamide, cisplatin, carboplatin, and antifolates.

The technology

Pemetrexed disodium is a multi-targeted anti-cancer antifolate agent that exerts its action by disrupting crucial folate-dependent metabolic processes essential for cell replication.

Pemetrexed disodium in combination with cisplatin is indicated for the treatment of chemotherapy naive patients with unresectable malignant pleural mesothelioma.

Cisplatin is a platinum-based chemotherapeutic agent that has antitumour activity, either as a single agent or in combination, for a number of different cancers. It is available in the UK from APS, Mayne and Bristol-Myers Squibb.

In patients treated for malignant pleural mesothelioma, the recommended dose of pemetrexed is 500mg/m^2 of body surface area (BSA) administered as an intravenous infusion over 10 minutes on the first day of each 21-day cycle. The recommended dose of cisplatin is 75mg/m2 BSA infused over two hours approximately 30 minutes after completion of the pemetrexed infusion on the first day of each 21-day cycle.

Intervention(s)	Pemetrexed disodium and cisplatin in combination
Population(s)	Chemotherapy naive patients with unresectable malignant pleural mesothelioma.
Standard comparators	Cisplatin Other commonly-used alternatives (see “Questions” at the end of this draft scope). Supportive care

Outcomes	The outcome measures to be considered include: • Overall survival • Toxicity and adverse effects of treatment • Symptom palliation • Health-related Quality of Life • Performance status • Tumour response • Progression free survival
Economic analysis	Ideally, the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. Costs should be considered from an NHS and Personal Social Services perspective.
Other considerations	• Relevant sub-group analyses should be undertaken (see "Questions" at the end of this draft scope) • Different treatment stopping rules should be considered with any economic evaluation (see "Questions" at the end of this draft scope). • Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: None Related Clinical Guidelines: None

Questions for consultation
NICE will be pleased to receive any comments and suggestions on any of the above text. However, comments are particularly invited on the following:

Which chemotherapy regimens are commonly currently used in England and Wales?.

Do identifiable patient sub-groups exist? If so, what are they?

What, if at all, are considered to be clinically appropriate stopping rules for treatment? (For example, can response and/or survival at the end of therapy be predicted from the response after one, two or three cycles of combination therapy? Does patient-level data exist that would answer this question?)