

# Considered Judgement Form

*This form is a checklist of issues that may be considered by the Purchasing Guidance Advisory Group when making purchasing recommendations.*

**Meeting date:** 19<sup>th</sup> of May, 2005

**Topic:** The effectiveness of pemetrexed in the treatment of mesothelioma

**Background and Purpose:** Malignant Pleural Mesothelioma (MPM) is an uncommon malignancy, often caused by exposure to asbestos (50-70% of cases<sup>1</sup>). Mesothelioma is the classic tumour associated with asbestos exposure, and has a latency period of 20-40 years or more from the time of first exposure.<sup>2</sup> Once a person is diagnosed with mesothelioma, their prognosis is often extremely poor, with a life expectancy of between 6 to 18 months (5-year survival <5%).<sup>1</sup> Until recently, no treatments have been shown to be able to cure this disease or extend life expectancy.

In August 2004, a new drug called pemetrexed (brand name ALIMTA) was registered for use in New Zealand for the treatment of malignant pleural mesothelioma in combination with cisplatin.

## 1. Effectiveness, Volume of Evidence, Applicability /Generalisability and Consistency

Comment here on the extent to which the service/product/ procedure achieves the desired outcomes. Specific reference needs to be made to safety. Report number needed to treat and harm where possible, any issues concerning the quantity of evidence and its methodological quality and the extent to which the evidence is directly applicable or generalisable to the New Zealand Population, and the degree of consistency demonstrated by the available evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence

One good quality randomised controlled trial has been published which shows that pemetrexed 500mg/m<sup>2</sup> + cisplatin 75mg/m<sup>2</sup> in combination with folic acid and vitamin B<sub>12</sub> is effective at prolonging life by an average of 2.8 months in patients who have malignant pleural mesothelioma. . Once folic acid and vitamin B12 were added, there was a significant reduction in toxicity in the intervention group. Forty one percent of patients in the intervention group responded to this treatment. This treatment was compared to 75mg/m<sup>2</sup> Cisplatin alone where only 17% responded to treatment.

Two case series have also been published which show variable response rates. One study reported that 14.1% of patients responded to pemetrexed alone, and the other reported that 32% of patients had partial response to a pemetrexed + carboplatin combination.

## 2. Cost

Comment on any economic costs associated with this service, product or procedure

There is currently no information in the literature relating to the cost-effectiveness of pemetrexed + cisplatin in the treatment of mesothelioma.

The current purchase price of pemetrexed is \$2241 per vial (GST exclusive). (For a 70kg patient, approximately two vials would be infused at each treatment time). Cisplatin is an extra \$143.80 per cycle.

PTAC have recommended that this be funded on The Pharmaceutical Schedule as a low priority. In reality this means it probably won't be funded in the short term.

### 3. Clinical impact

Comment on the clinical impact e.g. size of population, magnitude of effect, relative benefit over other management options, resource implications, balance of risk and benefit.

Treatment with Pemetrexed + cisplatin may extend a terminally ill person's life by an average of 3 months. This is the only treatment that has shown to be effective in the treatment of mesothelioma.

Alternatives include combinations of Gemcitabine, and Cisplatin or Mitomycin C, Vinblastine and Cisplatin, which have yet to be formally tested.

PHARMAC has estimated 30-40 cases per year for mesothelioma. Seven requests for pemetrexed funding have been received by ACC in the last 2 weeks.

### 4. Equity, Maori Health, Pacific Health, Acceptability

Comment on the extent to which the service, product or procedure reduces disparities in health status (equity of access, resources, health outcome), is consistent with the treaty of Waitangi and encourages Maori/ Pacific participation in providing and using service, product and procedures, and is consistent with values and expectations of New Zealanders.

The purchasing recommendation shall be applied equally across Maori, Pacific and ethnic populations.

### 5. Possible Purchasing Options

List the possible purchasing options.

**Option 1:** Don't purchase

**Option 2:** Purchase if prescribed

### 6. Evidence Statement

Summarise the advisory group's synthesis of evidence relating to this service, product or procedure, taking the above factors into account, and indicate the evidence level that applies.

There is evidence from one good quality randomised controlled trial that supports the use of Pemetrexed in combination with cisplatin, folic acid, and Vitamin B12 for the treatment of mesothelioma.

### 7. Purchasing Recommendations

What recommendation(s) does the advisory group draw from this evidence?

Purchase pemetrexed.

#### **Good practice points:**

Pemetrexed 500mg/m<sup>2</sup> + cisplatin 75mg/m<sup>2</sup> in combination with folic acid and vitamin B<sub>12</sub> should be funded for patients with asbestos-related malignant pleural mesothelioma. Each cycle should be given 21 days apart. If no clear clinical benefit is observed after 2 treatment cycles, treatment should be withdrawn.

Suggested prescribing criteria for consideration of funding from ACC:

1. the patient has a proven diagnosis of Mesothelioma of the pleura or peritoneum. Diagnosis should include both histological and radiological assessments.
2. The patient must have a performance status of 2 or better on the WHO scale (after any palliative

measures, including pleural drainage).

3. The patient must have adequate organ function including:

- i. Renal-calculated creatine clearance > 45mls/min.
- ii. Adequate bone marrow reserve-absolute neutrophil count >  $1.5 \times 10^9/L$  platelets >  $100 \times 10^9/L$  and haemoglobin > 90g/dcl.
- iii. Hepatic, bilirubin  $\leq 1.5$ , ALP  $\leq$  AST ALT  $\leq 3$ x upper limit or normal (ALP, ASP, ALT  $\leq 5$ x upper limit of normal is acceptable if there is tumour involvement).

4. Patients must have adequately treated and stable brain metastases

If the patient meets all of the above criteria, treatment for the above would include Pemetrexed base therapy, either in combination with Cisplatin or Carboplatin.

(Recommendation from Dr. Richard Sullivan, Clinical Director – Medical Oncology, Regional Cancer and Blood Service, Auckland Hospital).

\* Cisplatin, Folic acid and Vitamin B12 therapy are already available via The Pharmaceutical Schedule for which ACC has contributed a bulk fund for pharmaceuticals.

### **References**

1. Testa, J.R., H.I. Pass, and M. Carbone, ***Benign and malignant mesothelioma***, in ***Cancer: Principles and Practice of Oncology (ed 6)***, V.T. DeVita, S. Hellman, and S. Rosenberg, Editors. 2001, Lippincott, Williams & Wilkins: Philadelphia, PA. p. 1937-1969.