Pemetrexed (for MPM)

**Product:**
PEMETREXED (Alimta®)

**Class of drugs:**
Antineoplastic agent

**Indication:**
Treatment of malignant pleural mesothelioma (MPM)

**Manufacturer:**
Eli Lilly Canada Inc.

**Highlights of Recommendation:**
- Pemetrexed (Alimta), in combination with cisplatin (a chemotherapy agent), is used to treat malignant pleural mesothelioma (MPM), a type of lung cancer.
- Currently, there is no evidence that patients live longer or that their quality of life improves with standard chemotherapy regimens used to treat MPM.
- Studies suggest that survival in MPM patients treated with pemetrexed (Alimta) plus cisplatin may improve by 2.8 months versus those treated with cisplatin alone. However, studies also suggest that raltitrexed (a chemotherapy agent in a similar family to pemetrexed) plus cisplatin may also improve survival in patients suffering from MPM by 2.6 months versus cisplatin alone.
- The cost of pemetrexed (Alimta) is approximately $22,000 for a six-cycle course of treatment. Raltitrexed is currently reimbursed through the Cancer Care Ontario’s (CCO’s) New Drug Funding Program (NDFP) when given in combination with cisplatin, at an approximate cost of $3,000 for a six-cycle course of therapy.
- Overall, the Committee believes that pemetrexed (Alimta) and raltitrexed have similar clinical benefits for the treatment of MPM. Raltitrexed is already listed on the Formulary. Given that the cost of raltitrexed is approximately 15% of the cost of pemetrexed (Alimta), the Committee concluded that pemetrexed (Alimta) did not demonstrate good value-for-money. As an effective alternative is currently available on the NDFP Formulary, the Committee recommended that pemetrexed (Alimta) not be approved for funding under CCO’s NDFP Formulary.

**Background:**
Malignant pleural mesothelioma (MPM) is a locally invasive cancer linked to asbestos exposure. MPM is difficult to treat and may not respond to surgery, radiation, or drug therapy. Patients generally present with symptoms such as pain, shortness of breath, and cough. Patients generally do not do well and studies have estimated five-year overall survival of 1% or less, with median survival rates of less than eight months for patients receiving best supportive care. There are two related drugs that are recommended, in combination with cisplatin, for the treatment of MPM in patients whose tumour cannot be surgically removed or who are not candidates for curative surgery. Health Canada has approved pemetrexed (Alimta) for the treatment of MPM in combination with cisplatin. Raltitrexed is a similar drug that costs significantly less and works in the same manner. Although raltitrexed is not approved by Health Canada for MPM, it is a recommended therapy for MPM in Ontario, according to CCO’s Program in Evidence-based Care guideline. It is currently reimbursed through CCO’s NDFP when given in combination with cisplatin.

**CED Recommendation**
The CED recommended not to fund pemetrexed (Alimta) through Cancer Care Ontario’s New Drug Funding Program, on the basis that it does not provide value-for-money compared with existing alternatives on the Formulary.

**Executive Officer Decision**
Based on the CED’s recommendation, the Executive Officer decided not to list pemetrexed (Alimta) for the treatment of malignant pleural mesothelioma (MPM).

**Status**
No funding through Cancer Care Ontario’s New Drug Funding Program.

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Detailed Discussion:

- The manufacturer, Eli Lilly Canada Inc., asked the Ministry of Health and Long-Term Care to consider listing pemetrexed (Alimta) on the New Drug Funding Formulary (NDFP).
- The Committee to Evaluate Drugs has reviewed this product three times.

First Review – April 2005

- The evidence supporting treatment with pemetrexed (Alimta) comes from a randomized controlled trial comparing pemetrexed in combination with cisplatin, versus cisplatin alone, in patients with MPM. This trial reported response rates of 41% vs. 17%, p<0.001; time to progression (5.7 vs. 0.9 months, p = 0.001), and survival (12.1 vs. 9.3 months, hazard ratio 0.77, p=0.02) in favour of the combination arm.
- Grade 3 and 4 toxicities were higher in the combination arm: neutropenia (28% vs. 2%), thrombocytopenia (6% vs. 0%) and febrile neutropenia (2% vs. 0%). Two quality-of-life indices (dyspnea and pain) assessed using the Lung Cancer Symptom Scale were significantly improved with pemetrexed and cisplatin after six cycles of treatment (p=0.004 nd p=0.017, respectively).
- The Committee recommended that pemetrexed (Alimta) not be reimbursed through CCO’s NDFP.

Second Review – December 2005

- The manufacturer provided an updated pharmacoeconomic analysis for review.
- The Committee noted that a randomized Phase III study of cisplatin with or without raltitrexed in patients with MPM had been published. The reported response rates were 13.6% in the cisplatin arm versus 23.6% in the cisplatin plus raltitrexed arm. Median overall survival was 8.8 months in the cisplatin arm versus 11.4 months in the cisplatin plus raltitrexed arm, which was a statistically significant difference. The Committee noted that raltitrexed might have a better toxicity profile and in addition, cost less than pemetrexed.
- The Committee recommended that pemetrexed (Alimta) not be reimbursed at that time because it was not cost-effective.

Third Review – October 2006

- The Committee reviewed an updated pharmacoeconomic analysis.
- Raltitrexed had recently been approved and added to the NDFP Formulary for the treatment of MPM. The Committee believed that pemetrexed (Alimta) and raltitrexed, being of the same drug class, demonstrated evidence of similar clinical efficacy. The cost of raltitrexed is approximately 15% of the cost of pemetrexed (Alimta). The CED recommended that pemetrexed (Alimta) not be reimbursed because it was not found to be cost-effective.