Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: January 2016

Pemetrexed for maintenance treatment of non-small cell lung cancer

Product: pemetrexed (Alimta®)

Class of Drugs: folic acid antagonist

Reason for Use: Maintenance treatment of locally advanced or metastatic non-squamous non-small cell lung cancer (NS-NSCLC)

Manufacturer: Eli Lilly Canada Inc.

Date of Review: December 11, 2013

CED Recommendation

The CED noted that the use of pemetrexed (Alimta®) in the maintenance treatment of locally advanced or metastatic non-squamous non-small cell lung cancer (NS-NSCLC) has been shown to improve overall survival and progression-free survival compared to placebo. Due to concerns related to cost-effectiveness, the CED recommended that pemetrexed not be funded in this clinical setting. This recommendation is aligned with the pan-Canadian Oncology Review recommendation.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with the manufacturer to help address concerns raised by the CED, the Executive Officer decided to fund pemetrexed (Alimta®) for maintenance treatment of locally advanced or metastatic NS-NSCLC according to specific criteria.

Funding Status*

Funded through Cancer Care Ontario's New Drug Funding Program according to specific criteria.

** This information is current as of the posting date of the document. For the most up-to-date information on Executive Officer decision and funding status, see: www.health.gov.on.ca/en/pro/programs/drugs/status_single_source_subm.aspx.*

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Highlights of Recommendation:

- The PARAMOUNT study showed that pemetrexed maintenance therapy improved overall survival and progression-free survival compared to placebo.
- In the study, the use of pemetrexed compared to placebo did not have a negative impact on patients' quality of life.
- The overall safety of pemetrexed was considered acceptable.
- At the recommended dose, the average cost per 28-day course of pemetrexed is $4862. The use of pemetrexed maintenance therapy was not considered to be cost-effective.

Background:

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. It usually grows and spreads more slowly than small cell lung cancer. There are three common types of NSCLC: adenocarcinomas, squamous cell carcinomas, and large cell carcinomas.

The standard first-line treatment for advanced NSCLC is platinum-based doublet chemotherapy. The use of maintenace treatment following induction therapy with a platinum-based doublet has been evaluated in recent years to determine whether this strategy would improve survival and other clinical outcomes.

Detailed Discussions:

- For this evaluation, the CED took into consideration:
    - Findings from the pan-Canadian Oncology Drug Review (pCODR) and the recommendation of the pCODR Expert Review Committee;
    - Information in the manufacturer's submission;
    - Submission from one patient group received by pCODR.
    - Feedback from Cancer Care Ontario's Lung Disease Site Group.
- The CED evaluated one double-blind, phase III, placebo controlled trial, the PARAMOUNT study. The study compared pemetrexed plus best supportive care to placebo plus best supportive care for the maintenance treatment of patients with advanced (locally advanced or metastatic) non-squamous, non-small cell lung cancer (NS-NSCLC).
- All patients in the PARAMOUNT study received induction therapy with four cycles of pemetrexed plus cisplatin. Only those patients with stable disease and clinical status (ECOG performance status 0 or 1) after receiving the four induction cycles were permitted to receive pemetrexed maintenance therapy.
- The primary outcome of the PARAMOUNT study was investigator-assessed progression free survival (PFS). Overall survival (OS) was a secondary outcome. Median PFS was 4.1 vs. 2.8 months for pemetrexed compared to placebo, respectively (HR: 0.62, 95% CI, 0.49 to 0.79) and median OS was 13.9 vs. 11.0 months (HR: 0.78, 95% CI, 0.64 to 0.96, p = 0.0199), respectively. The CED noted that the improvement in OS, although modest, could be considered significant in the cancer treatment setting.

- There was some uncertainty as to whether the observed improvements could be the result of differences in subsequent therapies. Some patients in the placebo group crossed over to receive pemetrexed after their disease had progressed, making it difficult to determine the true benefit of pemetrexed maintenance treatment.
- There was a similar decline in patients' quality of life (QOL) in both the pemetrexed and placebo groups, suggesting that pemetrexed did not negatively impact QOL.
- The observed adverse events with pemetrexed in the study were consistent with the known toxicity profile of pemetrexed.
- At the submitted price, pemetrexed costs $4.29 per mg. At the recommended dose of 500mg/m^2 on day 1 of every 21 day cycle, the average cost per 28-day course is $4862. Pemetrexed maintenance treatment was not considered to be cost-effective.
- The CED reviewed two patient group submissions received by pCODR. The patient submissions highlighted the impact of the disease and patients' wishes for additional therapeutic options, including treatments that delay disease progression.
- Overall, the PARAMOUNT study demonstrated that pemetrexed maintenance therapy improves overall survival and progression-free survival. This treatment was not considered to be cost-effective.

Committee to Evaluate Drugs (CED)

The Committee to Evaluate Drugs (CED) is comprised of practicing physicians, pharmacists, health economists, and patient representatives. In conducting its review, the CED considers data contained in the drug manufacturer's submission, input provided by patient groups, findings from the national Common Drug Review and the pan-Canadian Oncology Drug Review, and other scientific information as necessary.

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