Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: January 2016

Afatinib

Product: afatinib (Giotrif®)

Class of Drugs: tyrosine kinase inhibitor (TKI)

Reason for Use: non-small cell lung cancer (NSCLC)

Manufacturer: Boehringer Ingelheim Canada Ltd.

Date of Review: May 14, 2014

CED Recommendation

The CED did not recommend afatinib (Giotrif®) for funding to treat non-small cell lung cancer (NSCLC) due to concerns with cost-effectiveness compared to another treatment, gefitinib, also used to treatment NSCLC. Afatinib has been shown to improve progression-free survival when compared with chemotherapy.

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 afatinib (Giotrif®) for the treatment of non-small cell lung cancer (NSCLC) according to specific criteria.

Funding Status*

Funded through the Ontario Drug Benefit's Exceptional Access Program according to specific criteria.

(EAP criteria can be found at: http://www.health.gov.on.ca/en/pro/programs/drugs/eap_criteria.aspx)

* *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:

- Two randomized controlled studies showed that afatinib improved progression-free survival when compared with cisplatin-based chemotherapy in patients with previously untreated epidermal growth factor receptor (EGFR) mutation-positive advanced non-small cell lung cancer (NSCLC).
- The adverse effects with afatinib were considered to be manageable.
- There are no randomized controlled trials comparing afatinib to gefitinib (a standard first-line treatment).
- Afatinib costs $2240 per 28-day course of therapy. Afatinib has not been shown to be cost-effective when compared with gefitinib, which costs $2052 per 28-day course.

Background:

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. About 10% of patients with NSCLC have a mutation in the epidermal growth factor receptor (EGFR) gene.

Afatinib is an EGFR tyrosine kinase inhibitor (TKI). It is used in the first-line treatment (i.e., as initial therapy) of EGFR mutation-positive advanced NSCLC.

The Ontario Drug Benefit Program funds two other EGFR TKIs, gefitinib and erlotinib.

Detailed Discussions:

- For this evaluation, the CED considered:
    - Findings from the pan-Canadian Oncology Drug Review (pCODR) and the recommendation of the pCODR Expert Review Committee;
    - Information in the manufacturer's submission;
    - Two patient group submissions;
    - Feedback from Cancer Care Ontario's Lung Disease Site Group.
- Two randomized controlled trials, LUX-Lung 3 and LUX-Lung 6, compared afatinib to cisplatin-based chemotherapy in patients with previously untreated locally advanced or metastatic lung cancer with EGFR mutations.
- The primary outcome of both studies was independently-assessed progression-free survival (PFS). After a median follow-up of 16.4 months (LUX-Lung 3) and 16.6 months (LUX-Lung 6), the two studies reported statistically and clinically significant differences in independently- and investigator-assessed PFS in favour of afatinib compared to cisplatin-based chemotherapy. The median PFS was 4 - 5 months longer in the afatinib groups.
- Neither study demonstrated a statistically significant difference in overall survival (OS). The large numbers of chemotherapy patients who switched to TKI therapy after their disease progressed may have impacted the OS results.
- Patient-reported symptoms and health-related quality of life measures were either improved or unchanged with afatinib compared to cisplatin-based chemotherapy.

- Serious adverse effects (AEs) were similar between the afatinib and chemotherapy groups. Afatinib was associated with substantially more diarrhea and skin-related AEs, all of which are considered to be manageable.
- There are no randomized controlled studies comparing afatinib to gefitinib or erlotinib. The relative efficacy and safety and the optimal sequencing of the various TKI treatments are unknown. The ongoing LUX-Lung 7 study, which compares afatinib to gefitinib, could provide valuable data.
- Afatinib costs $2240 per 28-day course of therapy. Afatinib has not been shown to be cost-effective when compared with gefitinib, which costs $2052 per 28-day course.
- Two patient group submissions identified concerns with current treatment options and noted that access to more alternatives is important.
- Overall, although afatinib has been shown to improve progression-free survival when compared with cisplatin-based chemotherapy, this treatment has not been shown to be cost-effective compared with gefitinib.

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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