Committee to Evaluate Drugs (CED)

Recommendations and Reasons

Document Posted: May 2015

Pertuzumab/Trastuzumab

Product: Pertuzumab/Trastuzumab (Perjeta®-Herceptin® Combo Pack)

Class of Drugs: anti-HER2 monoclonal antibodies

Reason for Use: HER2-positive metastatic breast cancer

Manufacturer: Hoffmann-La Roche Limited

Date of Review: September 11, 2013

CED Recommendation

The CED recommended pertuzumab/trastuzumab (Perjeta®-Herceptin® Combo Pack) not be funded for the treatment of HER2-positive metastatic breast cancer. The CED noted that this treatment provides survival benefits but is not cost-effective compared to other products funded for this use.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with manufacturer to help address concerns raised by the CED, the Executive Officer decided to fund pertuzumab/trastuzumab (Perjeta®-Herceptin® Combo Pack) for the treatment of HER2-positive metastatic breast cancer 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.*

Ontario

Highlights of Recommendation:

- Pertuzumab is indicated for use in combination with trastuzumab and docetaxel for the treatment of patients with HER2- positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. Pertuzumab is only available in a combination kit with trastuzumab.
- The results of the CLEOPATRA study showed that the addition of pertuzumab to trastuzumab and docetaxel chemotherapy regimens was found to provide clinically significant improvements in both progression-free survival and overall survival in HER2-positive locally recurrent or metastatic breast cancer when compared to trastuzumab plus docetaxel alone.
- The overall safety of pertuzumab, including its potential effect on the heart, was found to be acceptable.
- At the recommended dose, the average cost per 28-day course of pertuzumab/trastuzumab Combo Pack is $8,417. Based on information submitted by the manufacturer and analyses conducted by the pan-Canadian Oncology Drug Review (pCODR), the addition of pertuzumab to trastuzumab and docetaxel could not be considered cost-effective. The price of pertuzumab would need to be significantly reduced to bring its cost-effectiveness to an acceptable level.
- Overall, based on the results of the CLEOPATRA study, the addition of pertuzumab to trastuzumab and docetaxel was found to provide clinically significant improvements in both progression-free survival and overall survival in HER2-positive locally recurrent or metastatic breast cancer when compared to trastuzumab plus docetaxel alone. Pertuzumab is not cost-effective.

Background:

Breast cancer is the most commonly diagnosed malignancy in Canadian women, with an estimated incidence of 23,600 new cases in Canada and an estimated 5,100 Canadian women dying from breast cancer in 2011.

Approximately 15-20% of all breast cancers have gene amplification or over-expression (or both) of human epidermal growth factor receptor 2 (HER2), resulting in more aggressive cancer and a poor prognosis. Trastuzumab (Herceptin®) is the first agent developed to target the HER2 pathway, and trastuzumab in combination with a taxane (e.g. docetaxel) is now recommended as first-line therapy for women with HER2/neu-overexpressing metastatic breast cancer (mBC). Within one year of starting treatment, the majority of patients with mBC initially responding to trastuzumab will experience disease progression.

More recently, a new class of agents targeting HER2 has been developed (HER dimerization inhibitors). Pertuzumab (Perjeta®) is a recombinant humanized monoclonal antibody and is indicated for use in combination with trastuzumab and docetaxel for the treatment of patients with HER2- positive mBC who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

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.
    - Patient group submissions to pCODR.
    - Feedback from Cancer Care Ontario's Breast Disease Site Group.
- One randomized controlled trial, the CLEOPATRA study, was included in the pCODR systematic review and evaluated by the CED. The results demonstrated a statistically significant improvement in the primary endpoint, progression-free survival (PFS), of 6.1 months for the pertuzumab arm compared to the placebo arm (median 18.5 versus 12.4 months, respectively; HR 0.62 CI 0.51-0.75; $p<0.001$).
- CLEOPATRA evaluated overall survival (OS) as a secondary endpoint. The final analysis of OS demonstrated a statistically significant difference in favour of the pertuzumab arm (median not reached) compared to the placebo arm (median 37.6 months; HR 0.66 95% CI 0.52-0.84; $p=0.0008$).
- Health-related quality of life (QOL) outcomes appeared similar between the two treatment arms, suggesting that the addition of pertuzumab did not decrease QOL. The QOL results were available only in abstract form and no details were available. The final study publication would be required to confirm this finding.
- The CLEOPATRA study provided evidence for the effectiveness of pertuzumab in combination with trastuzumab and docetaxel. In Ontario, a number of different chemotherapy regimens are often used in combination with trastuzumab. As the choice of chemotherapy does not likely impact a patient's overall clinical response and is often used interchangeably, it was considered reasonable to use pertuzumab in combination with any chemotherapy, such as any taxane or vinorelbine.
- The number of deaths and rates of withdrawal due to adverse events were similar between the pertuzumab group and the placebo group. Although more patients receiving pertuzumab experienced side effects, they were thought to be manageable and the overall tolerability of pertuzumab, including its potential effect on the heart, was considered acceptable.
- At the list price, pertuzumab-trastuzumab Combo Pack costs $6,448. At the recommended dose of 420 mg pertuzumab and 6mg/kg trastuzumab every 3 weeks, the average cost per 28-day course is $8,417. For the recommended loading dose of 840mg pertuzumab and 8mg/kg trastuzumab, the average cost for the first month is $13,031. Based on information submitted by the manufacturer and analyses conducted by the pan-Canadian Oncology Drug Review (pCODR), the addition of pertuzumab to trastuzumab and docetaxel could not be considered cost-effective. The price of pertuzumab would need to be significantly reduced to bring its cost-effectiveness to an acceptable level.
- Overall, based on the results of the CLEOPATRA study, the addition of pertuzumab to trastuzumab and docetaxel was found to provide clinically significant improvements in both progression-free survival and overall survival in HER2-positive locally recurrent or

metastatic breast cancer when compared to trastuzumab plus docetaxel alone. Pertuzumab is not 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.

For more information, please contact:

Ministry of Health and Long-Term Care

Ontario Public Drug Programs

Hepburn Block, 9th Floor

80 Grosvenor Street, Queen's Park

Toronto, Ontario M7A 1R3

www.health.gov.on.ca/en/pro/programs/drugs/