Gemcitabine (for metastatic breast cancer)

Product:
GEMCITABINE (Gemzar®)

Class of drugs:
Antineoplastic agent

Indication:
Treatment of metastatic breast cancer

Manufacturer:
Eli Lilly Canada Inc.

Highlights of Recommendation:
- Gemcitabine (Gemzar) is a chemotherapy used in the treatment of various types of cancer. This particular review examined the use of gemcitabine (Gemzar) in the treatment of metastatic (advanced) breast cancer.
- Gemcitabine (Gemzar) as standalone therapy has not been shown to provide significant benefit compared to other standard treatments for metastatic breast cancer. Evidence of efficacy comes from studies where gemcitabine (Gemzar) was used in combination with other chemotherapies.
- In one study, patients who received gemcitabine (Gemzar) plus paclitaxel survived for three months longer than patients who received paclitaxel alone. Results from this study were not helpful in establishing the therapeutic value of gemcitabine. This is because the study had used paclitaxel as a comparator, while the standard therapy used in Canada is docetaxel. A study evaluating whether gemcitabine (Gemzar) provides added benefits compared with docetaxel would have been more informative.
- A second study compared combination gemcitabine (Gemzar) plus docetaxel versus combination capecitabine plus docetaxel in the treatment of metastatic breast cancer. This study reported no difference in efficacy between the two treatment regimens.
- The most common side effects of gemcitabine (Gemzar) are increased liver enzyme levels, nausea, vomiting, fever and rash.
- The cost of gemcitabine (Gemzar) in combination with either docetaxel or paclitaxel ranges from $1,900 to $2,300 per cycle. The manufacturer did not submit adequate economic data for the Committee to determine whether this drug provides value for money.

Overall, the Committee noted that there is no evidence gemcitabine (Gemzar) provides added clinical benefit over the current standard treatment. Relevant economic information was also lacking to establish the cost-effectiveness of this drug.

Background:
Breast cancer is one of the most common cancers diagnosed among Canadian women. Metastatic breast cancer is the most advanced stage of breast cancer. The term “metastatic” describes cancer that has spread from the original tumour site to distant organs.

Most women in Ontario who develop advanced breast cancer are treated with hormonal therapy (if the disease is “hormone-sensitive”) or single agent chemotherapy. Women are usually offered anthracycline chemotherapy (e.g. doxorubicin, epirubicin) if they have not yet tried this class of treatment. In patients who have previously received anthracyclines, a taxane treatment (docetaxel or paclitaxel) is used. For patients whose disease has progressed after anthracyclines, or has progressed rapidly, combination chemotherapy with more than one cancer drug may be considered under certain circumstances.

CED Recommendation
The CED recommended that gemcitabine (Gemzar) not be funded through Cancer Care Ontario’s New Drug Funding Program (NDFP), on the basis that this drug’s therapeutic and economic value relative to alternative treatments could not be established.

Executive Officer Decision
Based on the CED’s recommendation, the Executive Officer decided not to list gemcitabine (Gemzar) for the treatment of metastatic breast cancer.

Status
No funding through Cancer Care Ontario’s New Drug Funding Program.
Detailed Discussion:

- The Committee reviewed gemcitabine (Gemzar) for the treatment of metastatic breast cancer on two occasions, initially in October 2006 and again in June 2007.
- The Committee reviewed a randomized controlled study (reported by O’Shaughnessy et al., Albain et al., and Moinpour et al. at the 2003 and 2004 American Society of Clinical Oncology Annual Meeting) that compared combination gemcitabine/paclitaxel against paclitaxel alone for the treatment of metastatic breast cancer in patients who have received prior anthracycline therapy. The study reported a 3 month overall survival improvement in the gemcitabine/paclitaxel arm versus the paclitaxel arm. The Committee noted that the results of this study was not informative because paclitaxel was used as a comparator. A more relevant comparator for the evaluation of gemcitabine (Gemzar) is docetaxel because a recent study demonstrated better efficacy with docetaxel monotherapy compared with paclitaxel monotherapy.
- The Committee also reviewed a study that compared combination gemcitabine/docetaxel with combination capecitabine/docetaxel in women with metastatic breast cancer who had received prior anthracycline therapy. This study found no significant difference in efficacy between the two treatment regimens in terms of objective response rate, progression-free survival, duration of response, or time-to-progression.
- The most common side effects of gemcitabine (Gemzar) are increased liver enzyme levels (68%), nausea and vomiting (64%), fever (37%) and rash (25%).
- The cost of gemcitabine (Gemzar) therapy in combination with either docetaxel or paclitaxel ranges from $1,900 to $2,300 per cycle.
- The manufacturer submitted a pharmacoeconomic analysis for combination gemcitabine/paclitaxel. As previously indicated, this is uninformative, as paclitaxel is not a relevant comparator. The manufacturer did not provide sufficient pharmacoeconomic data for an evaluation of the cost-effectiveness of combination gemcitabine/docetaxel.
- Overall, the Committee noted that there is no evidence gemcitabine (Gemzar) provides added clinical benefit over the current standard treatment. Relevant economic information was also lacking to establish the cost-effectiveness of this drug.
- The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as is done for all other cancer drug treatments.

Cancer Care Ontario (CCO) Information:

Information on CCO chemotherapy regimens for Breast Cancer is available at: http://www.cancercare.on.ca/index_chemoRegimensbyDisease.htm

The Breast Disease Site Group (DSG) Program in Evidence-based Care (PEBC) guideline for gemcitabine (Gemzar) in the treatment of metastatic breast cancer is available at: http://www.cancercare.on.ca/index_breastCancerGuidelines.htm

For more information, please contact:

Ministry of Health and Long-Term Care
Ontario Public Drug Programs

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
or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html