Fulvestrant

Product:
FULVESTRANT (Faslodex®)
50mg/mL injection

Class of drugs:
Hormonal (anti-estrogen) agent

Indication:
Treatment of metastatic breast cancer

Manufacturer:
AstraZeneca Canada Inc.

CED Recommendation-

The CED recommended that fulvestrant (Faslodex) 50mg/mL injection not be funded through the Ontario Drug Benefit Formulary, on the basis that there is no clinical evidence supporting its use as a last resort prior to chemotherapy, or that it increases survival rates.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided not to fund fulvestrant (Faslodex®) 50mg/mL injection on the Ontario Drug Benefit Formulary.

Status

No funding through the Ontario Public Drug Programs.

Highlights of Recommendation:

- Fulvestrant is used to treat breast cancer that has spread beyond the original tumour site, in post-menopausal women who have hormone-receptor positive breast cancer and who have failed previous treatments with hormonal agents. The manufacturer has requested fulvestrant be funded as fourth-line therapy after all other hormonal therapies have been exhausted.
- Current clinical evidence looks at the use of fulvestrant as second or third therapy to treat breast cancer that has spread beyond the original tumour site, in patients who have tested positive for hormone receptors. Based on this evidence, fulvestrant would be used as an alternative to anastrozole or exemestane, two other anti-cancer agents in the class of drugs known as aromatase inhibitors.
- The manufacturer submitted a cost-benefit analysis based on the assumption that fulvestrant would be used as a fourth-line therapy to delay the use of intravenous chemotherapy. There is no clinical trial evidence to support this sequence of treatment.
- **Overall, the Committee noted that the current evidence supports using fulvestrant instead of anastrozole or exemestane for locally advanced or metastatic breast cancer as second- or third-line therapy. There is no currently available clinical trial evidence to support the manufacturer's request to fund fulvestrant as the fourth or last resort before chemotherapy for the treatment of metastatic breast cancer.**

Background:

Breast cancer is the most common cancer among Canadian women. In Ontario, about 8,400 women are diagnosed with breast cancer every year; about 10 percent will develop metastatic disease, advanced breast cancer that has spread beyond the original tumour site. About 3 percent will already have metastatic breast cancer by the time they are diagnosed.

Most women in Ontario who develop advanced breast cancer will be treated with either single-agent chemotherapy or oral agents that block the action or reduce the levels of estrogen. Many breast cancers have hormone receptors (hormone-receptor positive disease) and growth of the cancer cells can be stimulated by hormones such as estrogen.

The hormonal agent, tamoxifen, blocks the actions of estrogen and stops cancer cells from growing. Other hormonal agents, the aromatase inhibitors (such as anastrozole and letrozole) work by blocking specific enzymes involved in estrogen production, thereby decreasing the levels of estrogen.

Fulvestrant is a hormonal agent which is administered once a month as an intramuscular injection. Fulvestrant is indicated for the hormonal treatment of locally advanced or metastatic breast cancer in postmenopausal women whose disease has progressed following prior hormonal therapy.

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Detailed Discussion:

- The manufacturer, AstraZeneca, asked the Ontario Ministry of Health and Long-Term Care to list fulvestrant as a Limited Use benefit on the Ontario Drug Benefit Formulary, for hormonal treatment of locally advanced or metastatic breast cancer in post-menopausal women whose disease has progressed or recurred and who have exhausted all other reasonable oral hormonal therapies, and in whom chemotherapy is the remaining option for treatment.
- The CED examined three Phase III trials (Chia et al. J Clin Onco 2008; Howell et al. J Clin Oncol. 2004; Osborne et al. J Clin Oncol. 2004) comparing single-agent fulvestrant to third-generation aromatase inhibitors (anastrozole and exemestane) in patients with tumour progression on prior hormonal therapy.
- The CED noted that the published data support the equivalence of fulvestrant with anastrozole and exemestane.
- An analysis of the combined data from two of the three trials did not demonstrate superiority of fulvestrant over anastrozole, and found no significant differences in efficacy, including the primary endpoint of time to progression of the disease.
- One of the three clinical trials found no significant differences in efficacy, tolerability, and quality of life endpoints in comparison to exemestane.
- There is no clinical trial evidence with respect to the sequence of fulvestrant therapy to support the manufacturer's request to fund fulvestrant as a last option, after all other oral treatments but prior to intravenous chemotherapy.
- The side effect profile of fulvestrant is similar to that of anastrozole. Side-effects include nausea, vomiting, constipation, diarrhea, abdominal pain, headache, back pain, hot flashes, and sore throat, as well as hair loss, and weight gain.
- Because fulvestrant is administered by intramuscular injection, mild transient pain and inflammation also occur at the injection site.
- The pharmacoeconomic analysis submitted by the manufacturer assumes that the treatment with fulvestrant would delay the need for intravenous chemotherapy and for palliative care. However, there is no evidence to demonstrate a survival benefit once aromatase inhibitors fail.
- **Overall, the CED noted that the current evidence supports using fulvestrant as second or third-line alternative therapy to anastrozole or exemestane for locally advanced or metastatic breast cancer in postmenopausal women with hormone-receptor-positive breast cancer. There is no current clinical trial data supporting the use of fulvestrant as fourth-line therapy or indicating that it provides a survival benefit once all hormonal therapies have failed.**
- The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as it does for all cancer drug treatments.

Cancer Care Ontario (CCO):

Information on CCO chemotherapy regimens for breast cancer is available at

http://www.cancercare.on.ca/toolbox/drugs/drugformulary/drugregimens/breastreg/

The Breast Disease Site Group (DSG) Program in Evidence-based Care (PEBC) guidelines for the treatment of metastatic breast cancer is available at:

http://www.cancercare.on.ca/cms/one.aspx?pageId=10193

CEDAC Recommendation:

(http://www.cadth.ca/index.php/en/cdr/recommendations)

The Canadian Expert Drug Advisory Committee (CEDAC) did not review fulvestrant (Faslodex) 50mg/mL injection.

Ontario

Ministry of
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