

Letrozole

Product:

LETROZOLE (Femara®) 2.5 mg tablet

Class of drugs:

Aromatase inhibitor; anti-estrogen agent

Indication:

Adjuvant treatment of breast cancer

Manufacturer:

Novartis Pharmaceuticals

CED Recommendation

The CED recommended that letrozole (Femara) 2.5 mg tablet be listed on the Ontario Drug Benefit (ODB) Formulary as a Limited Use benefit, with criteria, on the basis that it delivers longer disease-free survival time than tamoxifen, an alternative therapy commonly used for the adjuvant treatment of breast cancer.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer has decided to list letrozole (Femara) on the ODB Formulary under Limited Use benefit.

Status

Funding available through the Ontario Public Drug Programs.

Highlights of Recommendation:

- ◆ Letrozole (Femara) is a drug used to treat breast cancer in women who have already experienced menopause.
- ◆ The drug is an alternative to tamoxifen therapy for patients with hormone-receptor positive breast cancer, meaning that estrogen or progesterone hormone may cause their tumours to grow.
- ◆ The Committee reviewed the results of a study that reported patients taking letrozole (Femara) experienced a longer cancer-free period than patients taking tamoxifen.
- ◆ The cost of letrozole (Femara) is similar to other medications in the same class.
- ◆ **Overall, the Committee noted that letrozole (Femara) delivered a longer disease-free period for patients than tamoxifen, and that the product demonstrated value for money.**
- ◆ The CED recommended that Ontario Public Drug Programs reimburse letrozole (Femara) for the treatment of early-stage breast cancer as a Limited Use benefit, with specified criteria. (Please refer to the "Detailed Discussion" section for details of the criteria.)
- ◆ The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as is done for all other cancer drug treatments.

Background:

Breast cancer is one of the most common cancers diagnosed among Canadian women. Despite slight declines in death rates over the past decade for women with breast cancer, one in nine Canadian women will develop breast cancer in their lifetime.

In most cases, breast cancer relies on estrogen to feed the growth of tumours. Tamoxifen is commonly used for hormone-receptor positive breast cancer. It is given as part of adjuvant therapy – additional potentially curative therapy to the primary treatment required for breast cancer, such as surgery.

Letrozole (Femara) is a drug used to treat the early stages of breast cancer in women who have already experienced menopause. It works by binding to an enzyme and blocking the production of estrogen, essentially starving a breast cancer tumour of the food it needs to grow.

The Ontario Public Drug Programs also reimburses letrozole (Femara) for the treatment of hormone-receptor positive breast cancer in women whose cancer has spread (metastasized) from its original site, or for post-menopausal women who have received five years of tamoxifen therapy.

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Detailed Discussion:

- ◆ The manufacturer, Novartis Pharmaceuticals, asked the Ontario Ministry of Health and Long-Term Care to change the status under which it reimburses letrozole (Femara) on the ODB Formulary, to extend its reimbursement to the treatment of hormone-receptor positive early-stage breast cancer in post-menopausal women.
- ◆ The Committee reviewed the BIG-1-98 trial as the key study that supports the use of letrozole in the adjuvant treatment of early-stage breast cancer, in hormone-receptor positive patients.
- ◆ According to the study, the disease-free survival period was longer for patients taking letrozole (Femara) (84% at five years) than for those taking tamoxifen (81.4% after five years).
- ◆ The Committee noted there was no significant benefit in overall survival in the letrozole (Femara) arm of the study, but there is supportive evidence that distant disease-free survival can be used as a surrogate marker for overall survival.
- ◆ Patients taking letrozole (Femara) may experience greater risk of cardiovascular toxicity than patients taking tamoxifen, while patients on tamoxifen experienced more thromboembolic events, hot flashes, night sweats, and vaginal bleeding.
- ◆ Overall, the Committee noted there was a clinically significant improvement in disease-free survival for letrozole (Femara) vs. tamoxifen. The Committee also accepted that disease-free survival is a valid surrogate marker for overall survival in breast cancer.
- ◆ The incremental cost-effectiveness ratio (ICER) varies depending on the nodal status of the patient. The ICER for letrozole (Femara) falls within the range where a therapy is typically considered cost-effective. As such, letrozole (Femara) for the adjuvant treatment of breast cancer appeared to demonstrate value for money.
- ◆ The CED recommended that letrozole (Femara) continue be funded as a Limited Use benefit, with the following additional criterion:
 - As an alternative to tamoxifen for the adjuvant treatment of post-menopausal women with hormone-receptor positive early breast cancer for a maximum of five years.

Cancer Care Ontario (CCO) Information:

Information on Cancer Care Ontario's chemotherapy regimens for breast cancer is available at:

http://www.cancercare.on.ca/index_chemoRegimensbyDisease.htm

The Cancer Care Ontario's Breast Cancer Disease Site Group (DSG) Program in Evidence-Based Care (PEBC) guideline for the use of chemotherapy in breast cancer is available at:

http://www.cancercare.on.ca/index_breastCancerGuidelines.htm

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee did not review letrozole (Femara).



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

For more information, please contact:

Ministry of Health and Long-Term Care
Ontario Public Drug Programs
415 Yonge Street, Suite 1601
Toronto, Ontario M5B 2E7
or click: www.moh.on.gov.ca/dss/ced