Regimen Monograph

A - Regimen Name

LETR Regimen

Letrozole

Disease Site	Breast
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	• For the first-line treatment of hormone-receptor positive advanced breast cancer in postmenopausal women • For the hormonal treatment of advanced/metastatic hormone-receptor positive breast cancer after relapse or disease progression, in women with natural or artificially-induced postmenopausal endocrine status, who have previously been treated with anti-estrogens
Supplementary Public Funding	**letrozole** ODB - General Benefit (letrozole) (ODB Formulary)

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B - Drug Regimen

letrozole	2.5 mg	PO	Daily

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Not applicable

Other Supportive Care:

- Assess patient's risk factors for osteoporosis and consider calcium and vitamin D supplements and bisphosphonates where appropriate. Refer patients to the Bone Health During Cancer Treatment pamphlet for more information.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Dosage in myelosuppression: No dosage adjustment required.

Hepatic Impairment

Hepatic Impairment	Letrozole Dose

Mild to Moderate (Child-Pugh Class A or Class B)	No dose adjustment needed, although exposure may ↑ by 37%.
Severe (Child-Pugh C)	No data. Monitor patients closely and consider dose modification.

Renal Impairment

Creatinine Clearance (mL/min)	Letrozole Dose
≥ 10	No dose adjustment needed.
< 10	No data. Consider potential benefit-risk carefully.

Dosage in the Elderly

No dosage adjustment required. Older patients have an increased risk of osteoporosis and fracture.

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F - Adverse Effects

Refer to letrozole drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Estrogen deprivation symptoms	• Fatigue • Headache, musculoskeletal pain • Edema	• ↑ Cholesterol • Dizziness • Constipation • Nausea, vomiting • Osteoporosis, fracture	• Arterial thromboembolism • Venous thromboembolism • Arrhythmia • Cardiotoxicity • Cataracts • Hypersensitivity • Rash

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G - Interactions

Refer to letrozole drug monograph(s) for additional details.

- Avoid concomitant use with tamoxifen, other anti-estrogens, estrogen-containing or estrogenic therapies due to the risk of decreased letrozole efficacy.

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H - Drug Administration and Special Precautions

Refer to letrozole drug monograph(s) for additional details.

Administration:

- Tablets should be taken with a glass of water, with or without food, at around the same time every day.
- Tablets should not be crushed or chewed.
- Missed doses should be taken as soon as possible, but should be skipped if within a few hours (e.g. within 2 or 3 hours) of the next planned dose. Do not double the dose due to over-proportionality of exposure at doses above 2.5 mg daily.
- Store tablets at room temperature (15-30°C).

Contraindications:

- Patients with known hypersensitivity to letrozole, or any of its components, or other aromatase inhibitors.
- Premenopausal women*
- Pregnant and/or breastfeeding women
- Patients under 18 years of age

**not receiving ovarian suppression*

Warnings/Precautions:

- Few men were included in clinical trials. Management of breast cancer in men are generally extrapolated from clinical trials in women.
- Letrozole is not indicated in hormone-receptor negative disease.

- Some brands contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

Pregnancy/Lactation:

- Letrozole is **contraindicated** in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least:
  - **20 days** after the last dose for females (product monograph recommendation) or
  - **6 months** after the last dose for males (general recommendation).
- Breastfeeding: **Contraindicated**
- Fertility effects: Probable

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Serum cholesterol and lipids evaluation; Baseline and as clinically indicated
- Bone mineral density; Baseline and as clinically indicated
- LH, FSH and/or estradiol levels (in patients whose menopausal status is unclear or who become amenorrheic after chemotherapy); Baseline and regularly during the first 6 months of treatment
- Clinical toxicity assessment of fatigue, estrogen deprivation symptoms, musculoskeletal, cardiovascular, thromboembolism, GI and GU effects, ophthalmic, dermatologic effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Dombernowsky P, Smith I, Falkson G, Leonard R et al. Letrozole, a new oral aromatase inhibitor for advanced breast cancer: double-blind randomized trial showing a dose effect and improved efficacy and tolerability compared with megestrol acetate. J Clin Oncol 1998;16:453-61.

Gershanovich M, Chaudri HA, Campos D, et al. Letrozole, a new oral aromatase inhibitor: randomized trial comparing 2.5 mg daily, 0.5 mg daily and aminoglutethimide in postmenopausal women with advanced breast cancer. Ann Oncol 1998;9:639-45.

Letrozole drug monograph. Ontario Health (Cancer Care Ontario).

Mouridsen H, Gershanovich M, Sun Y, Pérex-Carrion R et al. Superior efficacy of letrozole (femara) versus tamoxifen as first-line therapy for postmenopausal women with advanced breast cancer: results of a phase III study of the international letrozole breast cancer group. J Clin Oncol 2001;19:2596-606.

November 2020 Updated adverse effects and monitoring sections; expanded interactions, drug administration and special precautions sections

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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