Regimen Monograph

A - Regimen Name

TMXF Regimen

Tamoxifen

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	Treatment of estrogen receptor positive advanced breast cancer in women
Supplementary Public Funding	**tamoxifen** ODB - General Benefit (tamoxifen)

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B - Drug Regimen

tamoxifen	20 mg	PO daily

(Outpatient prescription in multiples of 10mg & 20mg tablets)

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until evidence of disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Not applicable

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and may be considered.

Dosage with toxicity

Toxicity	Action
Severe estrogen depletion symptoms	Consider short drug holiday and rechallenge
Arterial/Venous thromboembolism	Discontinue
Severe depression	Discontinue
Pancreatitis, pneumonitis, hepatotoxicity, severe hypercalcemia	Discontinue
Cataracts, retinopathy, corneal changes, severe myalgia	Consider discontinuing
Severe skin symptoms, porphyria cutanea tarda, cutaneous lupus erythematosus	Discontinue

Microvascular breast reconstruction	Consider temporary hold

Hepatic Impairment

Adjustment required, no details found

Renal Impairment

No adjustment required

Dosage in the Elderly

No adjustment required.

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F - Adverse Effects

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

Most Common Side Effects (>10%)	Less Common Side Effects, but may be Severe or Life-Threatening
• Estrogen withdrawal symptoms • Nausea, vomiting • Rash (may be severe) • Fluid retention • Vaginal discharge, bleeding • Fatigue	• Hypersensitivity • Arterial thromboembolism • Venous thromboembolism • Ocular disorders (retinopathy, cataracts, optic neuritis) • Endometrial hyperplasia, polyps • Pancreatitis • Pneumonitis • Secondary malignancies (including uterine sarcoma/endometrial cancer) • Tumour flare (including hypercalcemia) • Porphyria, cutaneous lupus

	erythematosus, cutaneous vasculitis • ↑ LFTs • Radiation recall reaction

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G - Interactions

Refer to tamoxifen drug monograph(s) for additional details

- Avoid concomitant use with potent CYP2D6 inhibitors (e.g. fluoxetine, paroxetine, quinidine, pimozide, perphenazine)
- Caution with the use of moderate CYP2D6 inhibitors (e.g. desipramine, haloperidol, citalopram, sertraline, hydroxyzine, amlodipine) and consider alternative drug options
- Do not coadminster with anastrozole or letrozole
- Exercise caution when given with CYP3A4 inducers
- May significantly increaase anticoagulant effect. Monitor prothrombin time; adjust anticoagulant dose as required
- Avoid concomitant use with drugs that prolong the QT interval

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H - Drug Administration and Special Precautions

Refer to tamoxifen drug monograph(s) for additional details

Administration

- Oral self-administration; drug available by outpatient prescription.
- Swallow whole with a glass of water, with or without food.
- Do not crush or chew the tablets.
- Take the dose at about the same time each day.

Contraindications/Precautions

- Patients with hypersensitivity to tamoxifen or any of its components.
- Use with extreme caution in patients with a history of significant thromboembolic disease.
- Some brands of tamoxifen contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- Use with caution in patients with pre-existing myelosuppression or depression.

- Consider temporary hold in patients undergoing delayed microvascular breast reconstruction.
- Tiredness and weakness have been reported. Caution when driving and operating machinery while such symptoms persist.

Pregnancy / Lactation

- Tamoxifen is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment and for **9 months** after the last dose.
- Breastfeeding is not recommended.
- Fertility effects are unknown.

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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

- Calcium, in patients with extensive bone metastases; for first few weeks then periodic
- Clinical assessment of toxicity - vaginal bleeding, ocular, thromboembolism, myalgia, tumour flare, GI and pulmonary effects, rash; at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- CBC; periodic
- Triglycerides and cholesterol in patients with pre-existing hyperlipidemia

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Kuss JT, Muss HB, Hoen H, et al. Tamoxifen as initial endocrine therapy for metastatic breast cancer: long term follow-up of two Piedmont Oncology Association (POA) trials. Breast Cancer Res Treat 1997 Feb;42(3):265-74.

Muss HB, Wells HB, Paschold EH, et al. Megestrol acetate versus tamoxifen in advanced breast cancer: 5-year analysis--a phase III trial of the Piedmont Oncology Association. J Clin Oncol 1988;6(7):1098-106.

Muss HB, Case LD, Atkins JN et al . Tamoxifen versus high-dose oral medroxyprogesterone acetate as initial endocrine therapy for patients with metastatic breast cancer. J Clin Oncol 1994;12:1630-8.

Sunderland MC, Osborne CK. Tamoxifen in premenopausal patients with metastatic breast cancer: a review. J Clin Oncol 1991 Jul; 9(7): 1283-97.

May 2022 Modified Pregnancy/lactation section

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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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