Regimen Monograph

A - Regimen Name

CM(PO) Regimen

Cyclophosphamide (oral)-Methotrexate (oral)

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 pretreated metastatic breast cancer
Supplementary Public Funding	**cyclophosphamide** ODB - General Benefit (cyclophosphamide - oral tablets) (ODB Formulary) **methotrexate** ODB - General Benefit (methotrexate - oral tablets) (ODB Formulary)

back to top

B - Drug Regimen

cyclophosphamide (Outpatient prescription in multiples of 25mg or 50mg tablets)	50 mg	PO	Daily
methotrexate (Outpatient prescription in multiples of 2.5mg tablets)	2.5 mg	PO	BID on Days 1 and 2 of each week

back to top

C - Cycle Frequency

CONTINUOUS TREATMENT

Until evidence of non-response or disease progression

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Low – No routine prophylaxis; PRN recommended

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

back to top

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 could be considered.

Dosage with toxicity

Hematologic Toxicities

Platelet count (x 10^9/L)		Neutrophil/granulocyte count (x 10^9/L)	Dose (as % of planned dose)
75 - 100	AND/OR	1 - 1.49	50%

< 75	AND/OR	<1	Hold and delay; restart at 50%

Hepatic Impairment

If Bilirubin > 3 x ULN, **OMIT** dose of Methotrexate

Renal Impairment

Creatinine clearance (mL/sec)	Dose
0.2 - 0.8	**REDUCE** Methotrexate to **50%** dose
< 0.2	**OMIT** Methotrexate dose

Cyclophosphamide: Renal failure may lead to the reduced excretion of metabolites and increased toxicity. Significant falls in clearance (25-80%) with increased exposure have been documented in patients with renal impairment. Dose reduction (25- 50%) should be considered in patients with mild to moderate renal impairment. Patients with moderate renal impairment receiving high doses or severe renally impaired patients (CrCl < 10 mL/min) are at particular risk and should be treated at a reduced dose and with extreme caution.

back to top

F - Adverse Effects

Refer to cyclophosphamide, methotrexate drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Nausea, vomiting (may be severe)	• Hypersensitivity

• Increased LFTs (may be severe) • Alopecia • Anorexia, weight loss • Diarrhea • Mucositis • Hand-foot syndrome • Myelosuppression +/- infection, bleeding (may be severe) • Rash (may be severe) • Fatigue	• Arterial thromboembolism • Venous thromboembolism • GI perforation • Prolonged QT interval • Leukoencephalopathy • Seizure • Nephrotoxicity • Pancreatitis • Pneumonitis • Vasculitis • Visual disorders • Secondary malignancy

back to top

G - Interactions

Refer to cyclophosphamide, methotrexate drug monograph(s) for additional details

back to top

H - Drug Administration and Special Precautions

Refer to cyclophosphamide, methotrexate drug monograph(s) for additional details

back to top

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

- Clinical toxicity assessment (including stomatitis and cystitis); at each visit
- CBC; baseline and before each cycle
- Baseline and regular liver function tests
- Baseline and regular renal function tests

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Administrative Information

Outpatient prescription for home administration

back to top

K - References

Colleoni M, Rocca A, Sandri M, et al. Low-dose oral methotrexate and cyclophosphamide in metastatic breast cancer: antitumor activity and correlation with vascular endothelial growth factor levels. Annals of Oncology; 2002. 13: 73-80.

Cyclophosphamide and methotrexate drug monographs, Cancer Care Ontario.

May 2019 Updated emetic risk category

back to top

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.

The information set out in the drug monographs, regimen monographs, appendices and symptom management

information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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back to top