Regimen Monograph

A - Regimen Name

AC Regimen

ADRIAMYCIN ® (DOXOrubicin)-Cyclophosphamide

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 advanced breast cancer

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B - Drug Regimen

DOXOrubicin	60 mg /m²	IV	Day 1
cyclophosphamide	600 mg /m²	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until evidence of non-response, disease progression or limited by cardiotoxicity risk

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D - Premedication and Supportive Measures

Antiemetic Regimen: High

Febrile Neutropenia Risk: Low

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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 are in use at some centres.

Dosage with toxicity

Hematologic Toxicities: See Appendix 6 for general recommendations.

Worst Toxicity Type / Counts (x 10^9/L) in Previous Cycle	**Doxorubicin (% previous dose)**	**Cyclophosphamide (% previous dose)**
Febrile Neutropenia Thrombocytopenic bleeding Grade 4 ANC ≥ 7 d	75%*	
Cardiotoxicity **	Discontinue	Caution
Grade 3 related non-hematologic / organ	75% for suspect drug(s) *	
Grade 4 related non-hematologic / organ	Discontinue	

* Retreat when toxicities have recovered to ≤ grade 2, platelets ≥ 100 x 10^9/L, and ANC ≥ 1.5 x 10^9/L.
** including any signs and symptoms of heart failure, greater than 10% decline in LVEF to below the lower limit of normal, a greater than 20% decline in LVEF from any level, or LVEF ≤ 45%.

Hepatic Impairment

Bilirubin		**AST/ALT**	**Cyclophosphamide**	**Doxorubicin**
			(% of previous dose)	
1-2 x ULN	AND	< 2 x ULN	100%	50%
2-4 x ULN	OR	2-4x ULN	Caution	25%
>4 x ULN	OR	>4 x ULN	Caution	Discontinue

Renal Impairment

Creatinine Clearance (mL/min)	Cyclophosphamide (% of previous dose)	Doxorubicin (% of previous dose)
>30-50	100%	100%
10-30	50-75%	100%
<10	50% or OMIT	100%

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F - Adverse Effects

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

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression ± infection • Nausea and vomiting • Alopecia • Mucositis • Diarrhea • Cystitis • ↑ LFTs • Anorexia • Reproductive risks	• Cardiotoxicity • Thromboembolism, DIC, VOD • Secondary leukemia or malignancies • SIADH • Pneumonitis • Pancreatitis • Rhabdomyolysis • Photosensitivity • Vesicant

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G - Interactions

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

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H - Drug Administration and Special Precautions

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

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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

- Clinical toxicity assessment (including GI, cardiotoxicity, local toxicity, cystitis, infection); at each visit
- CBC; baseline and before each cycle
- Baseline and regular liver function tests
- Baseline and regular renal function tests and urinalysis
- Cardiac examination especially with risk factors (including prior therapy with epirubicin, mitoxantrone, or other cardiotoxic drug), or a cumulative doxorubicin dose of > 450 mg/m^2
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	1 to 1.5 hours
Pharmacy Workload (average time per visit)	30.564 minutes
Nursing Workload (average time per visit)	56.667 minutes

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K - References

Fisher B, Brown AM, Dimitrov NV, et al. Two months of doxorubicin/cyclophosphamide with and without interval reinduction therapy compared with six months of Cyclophosphamide, Methotrexate and 5-Fluorouracil in node-positive breast cancer patients with tamoxifen non-responsive tumors: results from the NSABP B-15. J. Clin Oncol 1990 Sep; 8(9): 1483-96.

Nabholtz JM, Falkson C, Campos D, et al. Docetaxel and doxorubicin compared with doxorubicin and cyclophosphamide as first-line chemotherapy for metastatic breast cancer: results of a randomized, multicentre, phase III trial. J Clin Oncol 2003; 21: 968-75.

January 2018 removed dose rounding factor

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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.

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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