Regimen Monograph

A - Regimen Name

CYCLDOCE Regimen

DOCEtaxel-Cyclophosphamide

CYCLDOCE+TRAS Regimen

DOCEtaxel-Cyclophosphamide-Trastuzumab

Disease Site	Breast
Intent	Adjuvant
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 for node-positive and high risk node-negative early operable breast cancer. Trastuzumab may be used concurrently with or after completion of CYCLDOCE in HER-2 positive breast cancer.
Supplementary Public Funding	**trastuzumab** New Drug Funding Program (Trastuzumab (Biosimilar) - Adjuvant Treatment for Breast Cancer)

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B - Drug Regimen

Note: Different trastuzumab products are **not interchangeable**.

DOCEtaxel	75 mg /m²	IV	Day 1
cyclophosphamide	600 mg /m²	IV	Day 1

For patients with HER2 positive tumours, trastuzumab is given for one year starting either concurrently with or after completion of chemotherapy.

trastuzumab
Refer to TRAS (Breast - Adjuvant) regimen for details.

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For total of 4 cycles unless unacceptable toxicity occurs

Trastuzumab: Refer to TRAS (Breast - Adjuvant) regimen for details.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Febrile Neutropenia Risk: High

Primary prophylaxis with G-CSF is indicated for CYCLDOCE. Refer to the Febrile Neutropenia Guideline.

Other Supportive Care:

Dexamethasone 8 mg bid po for 3 days starting 1 day prior to docetaxel (prevent anaphylaxis / fluid retention.)

- Trastuzumab: Refer to Trastuzumab drug monograph for full details.

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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 could be considered. See appendix 6 for general recommendations.

Suggested dose levels for docetaxel are 75 mg/m^2, 55 mg/m^2, 40 mg/m^2
Suggested dose levels for cyclophosphamide are 600 mg/m^2, 450 mg/m^2, 300 mg/m^2
See TRAS (Breast - Adjuvant) regimen for details on trastuzumab dose modifications.

Dosage with toxicity

Worst Toxicity Type / Counts x 10^9/L		Worst Toxicity Type / Counts x 10^9/L	Cyclophosphamide*	Docetaxel *
Febrile Neutropenia or Grade 4 ANC ≥ 7 d	Or	Thrombocytopenic bleeding	Hold* and ↓ 1 dose level (or consider GCSF – for isolated neutropenia)	Hold * and ↓ 1 dose level (or consider GCSF – for isolated neutropenia)
Grade 3 rash	Or	Grade 3 neurotoxicity	100%	↓ 1 dose level.* Discontinue if recurs
Any occurrence of cystoid macular edema			No change	Hold and investigate; refer patient promptly to an ophthalmic examination. Discontinue if confirmed.
Other Grade 3 organ / non-hematologic			↓ 1 dose level*	↓ 1 dose level*
Cystitis			Consider dose reduction	No change
Grade 4 organ / non-hematologic			Discontinue	Discontinue
* Major organ toxicity should have recovered to ≤ grade 2 , ANC ≥ 1.5 x 10^9/L and platelets ≥ 100 x 10^9/L prior to retreatment				

Hepatic Impairment

	AST and/or ALT		ALP		Bilirubin	Cyclophosphamide (% usual dose)	Docetaxel (% usual dose)
Mild-moderate	> 1.5 x ULN	AND	> 2.5x ULN			No change	Do not treat
Severe	> 3.5 x ULN	OR	> 6x ULN	OR	> ULN	Caution	Do not treat. Discontinue if treatment already started.

Renal Impairment

Creatinine Clearance (mL/min)	Cyclophosphamide (% of previous)	Docetaxel (% of previous)
>50	100%	100%
10-50	↓ 1 level	100%
<10	↓ 2 levels or **OMIT**	100%

Dosage in the Elderly

For docetaxel, no adjustment required, but caution should be exercised in elderly patients with poor performance status.

For cyclophosphamide, no dose modification routinely required, but should be used with caution.

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F - Adverse Effects

Refer to DOCEtaxel, cyclophosphamide, (± trastuzumab) drug monograph(s) for additional details of adverse effects.

The following adverse effects table is related to **CYCLDOCE**. Refer to trastuzumab drug monograph for additional details on trastuzumab.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Alopecia • Myelosuppression ± infection,	• Neuropathy (may be severe)	• Rash (may be severe) • Hypersensitivity	• Arterial / venous thromboembolism • Arrhythmia, QT

bleeding (may be severe) • Nausea, vomiting • Fatigue	• Fluid retention • Mucositis • Diarrhea • Nail disorder (may be severe)	reaction (may be severe) • Musculoskeletal pain	prolongation • Cardiotoxicity • Eye disorders (including cystoid macular edema, conjunctivitis & tear duct obstruction) • Radiation / injection recall and injection site reaction • Hand foot syndrome • Delayed wound healing • Disseminated intravascular coagulation • RPLS • Seizure • Bladder fibrosis • Hemorrhagic cystitis • GI obstruction / perforation • ↑ LFTs • Secondary malignancy • Pancreatitis • Rhabdomyolysis • Nephrotoxicity • SIADH • Adult respiratory distress syndrome (ARDS), pneumonitis • Veno-occlusive disease

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G - Interactions

Refer to DOCEtaxel, cyclophosphamide (± trastuzumab) drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to DOCEtaxel, cyclophosphamide (± trastuzumab) drug monograph(s) for additional details

Note: Different trastuzumab products are **not interchangeable**.

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I - Recommended Clinical Monitoring

See TRAS (Breast - Adjuvant) regimen for details on trastuzumab

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

- CBC before each cycle
- Baseline and regular liver function tests
- Baseline and regular renal function tests and urinalysis
- Clinical toxicity assessment (including neurologic, musculoskeletal, hypersensitivity, GI, skin and nails, cystitis, fluid retention, infection, bleeding, fatigue, thromboembolism, musculoskeletal pain, ophthalmic, or respiratory 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

Approximate Patient Visit

CYCLDOCE	2 hours
CYCLDOCE+TRAS	First cycle: 3.5 hours; Subsequent cycles: 2.5 hours

Pharmacy Workload **(average time per visit)**

CYCLDOCE	38.085 minutes
CYCLDOCE+TRAS	47.174 minutes

Nursing Workload **(average time per visit)**

CYCLDOCE	59.167 minutes
CYCLDOCE+TRAS	79.167 minutes

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K - References

Jones S, Holmes FA, O'Shaughnessy JO, et al. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow-up of US oncology research trial 9735. JCO 2009; 27(8): 1177-83.

Jones SE, Mavin MA, Holmes FA et al. Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. JCO 2006; 24: 5381-7.

Cyclophosphamide, docetaxel, trastuzumab drug monographs, Cancer Care Ontario.

PEBC Advice Documents or Guidelines

- Optimal Systemic Therapy for Early Female Breast Cancer

February 2022 Removed trastuzumab EBP forms; updated Rationale and uses 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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