Regimen Monograph

A - Regimen Name

AC-PACL Regimen

ADRIAMYCIN ® (DOXOrubicin)-Cyclophosphamide then PACLitaxel

AC-PACL+TRAS Regimen

ADRIAMYCIN ® (DOXOrubicin)-Cyclophosphamide then PACLitaxel and Trastuzumab

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

for Breast Cancer)

back to top

B - Drug Regimen

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

AC: (x 4 cycles)

DOXOrubicin (Round to nearest 1mg)	60 mg /m²	IV	Day 1
cyclophosphamide (Round to nearest 10mg)	600 mg /m²	IV	Day 1

THEN

PACLITAXEL (Taxol®): (x 4 cycles)

PACLitaxel (Round to nearest 3mg)	175 mg /m²	IV over 3 hours	Day 1

For patients with HER2 positive tumours, **Trastuzumab** may be given for one year, starting either concurrently with Paclitaxel or after 4 cycles of Paclitaxel:

trastuzumab

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

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

AC X 4 cycles then Paclitaxel (Taxol®) X 4 cycles

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

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: High (AC)
Low (Paclitaxel)

Febrile Neutropenia Risk: Low

Other Supportive Care:

- Paclitaxel: Patients should be pretreated with a corticosteroid as well as an antihistamine and a H2 Blocker.
- For example:
- Dexamethasone 20mg PO 12 & 6 hours or 20mg IV 30 minutes before Paclitaxel administration
- Diphenhydramine 50mg IV 30 minutes before Paclitaxel administration
- Ranitidine 50mg IV 30 minutes before Paclitaxel administration

back to top

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.

Toxicity Type / Counts x 10^9/L		**Toxicity Type / Counts x 10^9/L**	**Doxorubicin (% previous dose)**	**Cyclophosphamide (% previous dose)**	**Paclitaxel (% previous dose)**
ANC <1.5	Or	Platelet < 100	Hold *		
Febrile Neutropenia, or Grade 4 ANC ≥ 7 d	Or	Thrombocytopenic bleeding	Hold* then 75% (or consider GCSF – for isolated neutropenia)		
ANC ≥ 1.5	And	Platelet ≥ 100	100%		
Toxicity Type / Counts x 10^9/L		**Toxicity Type / Counts x 10^9/L**	**Doxorubicin (% previous dose)**	**Cyclophosphamide (% previous dose)**	**Paclitaxel (% previous dose)**
Grade 3/4 Neurotoxicity			Not applicable		80%*
Grade 3 related organ			*75% for suspect drug(s). If cardiotoxicity, follow recommendations in doxorubicin and paclitaxel drug monographs.		
Grade 4 related organ			Discontinue		

*Retreat when toxicities have recovered to ≤ grade 2, platelets ≥ 100 x 10^9/L, and ANC ≥ 1.5 x 10^9/L.

Hepatic Impairment

Bilirubin		**AST/ALT**	**Cyclophosphamide**	**Doxorubicin**	**Paclitaxel**
			(% of previous / mg/m^2)		
1-2 x ULN	and/ or	-	100%	50%	100%
2-4 x ULN		2-4x ULN	Caution	25%	135mg/m^2
>4 x ULN		>4 x ULN	Caution	Discontinue	50mg/m^2 or OMIT

Renal Impairment

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

back to top

F - Adverse Effects

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

Refer to trastuzumab drug monograph for adverse effect details (not listed below).

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Nausea and vomiting • Cystitis • Myelosuppression ± infection • Stomatitis and diarrhea • Peripheral neuropathy • Hypersensitivity reactions (Paclitaxel) • Myalgia and arthralgia • Alopecia	• Cardiotoxicity • Secondary leukemia/malignancies • Arterial/Venous Thromboembolism • Pneumonitis • SIADH • DIC, Hemolytic Uremic Syndrome • Rhabdomyolysis • Pancreatitis, GI obstruction, perforation

back to top

G - Interactions

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

back to top

H - Drug Administration and Special Precautions

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

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

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, cardiotoxicity, local toxicity, cystitis, hypersensitivity, neuropathy, musculoskeletal, infection or diarrhea); at each visit
- CBC 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

back to top

J - Administrative Information

Approximate Patient Visit

AC-PACL	AC: 1 to 1.5 hours; Paclitaxel: 5 hours
AC-PACL+TRAS	AC: 1 to 1.5 hours; Paclitaxel: 5 hours; TRAS: First cycle - 1.5 hours; Subsequent cycles - 0.5 hour

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

AC-PACL	24.613 minutes
AC-PACL+TRAS	29.158 minutes

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

AC-PACL	55.75 minutes
AC-PACL+TRAS	65.75 minutes

back to top

K - References

Henderson IC, Beryy D, Demetri G, Cirrincione C, et al. Improved outcomes from adding sequential Paclitaxel but not from escalating Doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer. J Clin Oncol, 2003 Mar15;21(6):976-83

Tan-Chiu E, Yothers G, Romond EH, et al. Assessment of cardiac dysfunction in a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel, with or without trastuzumab as adjuvant therapy in node-positive, Human Epidermal Growth Factor Receptor 2-overexpressing breast cancer: NSABP B-31. J Clin Oncol. 2005; 23(31): 7811-9.

PEBC Advice Documents or Guidelines

- Optimal Systemic Therapy for Early Female Breast Cancer

February 2022 Removed trastuzumab EBP forms; updated Rationale and uses section

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.

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back to top