Regimen Monograph

A - Regimen Name

FEC-D Regimen

Fluorouracil-EPIrubicin-Cyclophosphamide then DOCEtaxel

FEC-D+TRAS Regimen

Fluorouracil-EPIrubicin-Cyclophosphamide then DOCEtaxel-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 treatment for node-positive and high risk node-negative early breast cancer. Trastuzumab may be used concurrently with docetaxel or after completion of docetaxel in HER-2 positive breast cancer.
Supplementary Public Funding	**trastuzumab** New Drug Funding Program (Trastuzumab (Biosimilar) - Adjuvant Treatment for Breast Cancer) (NDFP Website)

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B - Drug Regimen

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

FEC100: (x 3 cycles)

fluorouracil (Round to nearest 25mg)	500 mg /m²	IV	Day 1
EPIrubicin (Round to nearest 1mg)	100 mg /m²	IV	Day 1
cyclophosphamide (Round to nearest 10mg)	500 mg /m²	IV	Day 1

THEN
DOCETAXEL: (x 3 cycles)

DOCEtaxel (Round to nearest 1mg)	100 mg /m²	IV	Day 1

For patients with HER2 positive tumours, **Trastuzumab** may be given for one year, starting either with docetaxel or after completion of FEC-D.

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

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

FEC100 X 3 cycles then docetaxel for 3 cycles

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

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D - Premedication and Supportive Measures

Antiemetic Regimen:	High (FEC) Low (docetaxel)
Febrile Neutropenia Risk:	High Consider G-CSF prophylaxis for patients at high risk of febrile neutropenia. See G-CSF recommendations.

Other Supportive Care:

- Dexamethasone 8 mg bid po for 3 days starting 1 day prior to docetaxel (prevent anaphylaxis / fluid retention.)
- Consider filgrastim as primary prophylaxis for febrile neutropenia, especially during cycles 4 to 6 of FEC-D.
- 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.

Patients should be tested for DPD deficiency before starting treatment with fluorouracil. Refer to the DPD Deficiency Guidance for Clinicians for more information.

In patients with unrecognized DPD deficiency, acute, life-threatening toxicity may occur; if grade 2-4

acute toxicity develops, treatment should be stopped immediately and permanent discontinuation considered based on clinical assessment of the toxicities.

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

Dosage with toxicity

For any appearance of *cystoid macular edema*, hold **docetaxel** and investigate; refer patient promptly to an ophthalmic examination. Discontinue **docetaxel** if confirmed.

Worst Toxicity Type / Counts x 10^9/L		**Worst Toxicity Type/Counts x 10^9/L**	**Fluorouracil (% of previous dose)**	**Epirubicin (% of previous dose)**	**Cyclophosphamide (% of previous dose)**	**Docetaxel**
Febrile Neutropenia or Grade 4 ANC ≥ 7 d	Or	Thrombocytopenic bleeding	Hold * then 75% (or Hold* then start GCSF – for low ANC only)			
Grade 3 rash	Or	Grade 3 neurotoxicity	Not applicable			*75%. Discontinue if recurs
Other grade 3 organ/ non-hematologic			*75% for suspect drug(s). If cardiotoxicity, follow recommendations in epirubicin and docetaxel drug monographs.			
Grade 4 organ/ non-hematologic			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

Consider dose reductions for epirubicin if severe increases in transaminases occur.

AST and/or ALT		Alk Phosphate		Bilirubin	Docetaxel (% previous)	Cyclophosphamide (% previous)	Epirubicin (% previous)	Fluorouracil (% previous)
> 1.5 x ULN	AND	> 2.5 x ULN			Do not treat	100%	50%	---
>3.5 X ULN	OR	> 6 X ULN	OR	2-4 X ULN	Do not treat Discontinue* if treatment already started.	Caution	25-50%	---
				> 4 X ULN	Discontinue	Caution	Discontinue	Discontinue

*Discontinue if bilirubin > ULN and any AST/ALT, Alk phosp

Renal Impairment

Creatinine Clearance (mL/min)	Fluorouracil	Epirubicin	Cyclophosphamide (% previous dose)	Docetaxel
>50	100%	100%	100%	No change
30 – 50	100%	100%	75%	No change
10 – 30	consider dose ↓		75%	
< 10	↓ dose		50% or OMIT	

Dosage in the Elderly

Epirubicin and cyclophosphamide should be used with caution; no adjustment required.

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

For trastuzumab, no adjustment required; the risk of cardiac dysfunction and myelosuppression may be increased in elderly patients. The reported trials did not determine differences in efficacy between patients > 65 years versus younger patients.

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F - Adverse Effects

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

The following adverse effects table is related to **FEC-D**. 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 (may be severe) • Nausea, vomiting (more likely with FEC) • Myelosuppression ± infection, bleeding (may be severe) • ECG changes (mostly asymptomatic; more likely with FEC) • Fatigue (more likely with D) • Mucositis (more likely with FEC) • Urine discolouration (with FEC)	• Neuropathy (may be severe; more likely with D) • Rash /dry skin /photosensitivity (may be severe; more likely with D) • Fluid retention (more likely with D) • Diarrhea (may be severe) • Nail disorder (may be severe; more likely with D) • Eye disorders (conjunctivitis / tearing more likely with FEC)	• Hypersensitivity (may be severe; more likely with D) • Injection site reaction (more likely with FEC) • Anorexia (with FEC) • Musculoskeletal pain (more likely with D) • Hand-foot syndrome (more likely with FEC)	• Arterial / venous thromboembolism • Arrhythmia • Cardiotoxicity • Radiation/injection recall • Delayed wound healing • Disseminated intravascular coagulation • RPLS • Leukoencephalopathy, seizure • Extrapyramidal / cortical dysfunction • Acute cerebellar syndrome • Cystoid macular edema • Bladder fibrosis • Hemorrhagic cystitis • GI obstruction /

			perforation or hemorrhage • Secondary malignancy • ↑ LFTs • Pancreatitis • Rhabdomyolysis • Nephrotoxicity • SIADH • Adult respiratory distress syndrome (ARDS), pneumonitis • Hemolysis • Veno-occlusive disease

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to fluorouracil, EPIrubicin, cyclophosphamide, DOCEtaxel (± 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

- **FEC**

- CBC; baseline and before each cycle
- Baseline and regular liver and renal function tests and urinalysis
- Cardiac examination especially with risk factors (including prior therapy with Doxorubicin, Mitoxantrone or other cardiac drug), or a cumulative Epirubicin dose of > 900mg/m^2
- Clinical toxicity assessment (including infection, bleeding, GI, thromboembolism, respiratory, cardiotoxicity, local toxicity, cystitis); at each visit

Docetaxel

- CBC, including nadir counts; baseline and at each visit
- Liver function tests; baseline and routine
- Regular clinical assessments of infection, bleeding, neurotoxicity, fluid retention, hypersensitivity, lethargy, cutaneous reactions, thromboembolism, musculoskeletal pain , cardiovascular, ophthalmic, GI or respiratory effects

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

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J - Administrative Information

Approximate Patient Visit	
FEC-D	FEC: 1.5 hours; Docetaxel: 2 hours
FEC-D+TRAS	FEC: 1.5 hours; Docetaxel-Trastuzumab: 3.5 hours (1st cycle), 2.5 hours(subsequent cycles)
Pharmacy Workload **(average time per visit)**	
FEC-D	28.925 minutes
FEC-D+TRAS	33.22 minutes
Nursing Workload **(average time per visit)**	
FEC-D	57.917 minutes
FEC-D+TRAS	68.75 minutes

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K - References

Coudert B, Asselain B, Campone M, et al. Extended benefit from sequential administration of docetaxel after standard fluorouracil, epirubicin, and cyclophosphamide regimen for node-positive breast cancer: the 8-year follow-up results of the UNICANCER-PACS01 trial. Oncologist 2012;17(7):900-9.

Cyclophosphamide, epirubicin, fluorouracil and docetaxel drug monographs, Cancer Care Ontario.

Mardarnas Y, Dent SF, Husain SF, et al. Real-world experience with adjuvant FEC-D chemotherapy in four Ontario regional cancer centres. Current Oncology 2011;18(3):119-25.

Roché H, Fumoleau P, Spielmann M, et al. Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: the FNCLCC PACS 01 Trial. JCO 2006; 24(36):5664-71.

PEBC Advice Documents or Guidelines

- Optimal Systemic Therapy for Early Female Breast Cancer

April 2023 Updated DPD deficiency information in the Dose Modifications 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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