Regimen Monograph

A - Regimen Name

FEC50 Regimen

Fluorouracil-EPIrubicin-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

fluorouracil (Round to nearest 25 mg)	500 mg /m²	IV	Day 1
EPIrubicin (Round to nearest 1 mg)	50 mg /m²	IV	Day 1
cyclophosphamide (Round to nearest 10 mg)	500 mg /m²	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: High

Other Supportive Care:

Also refer to CCO Antiemetic Summary

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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.

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.

Dosage with toxicity

Hematologic Toxicities: See Appendix 6 for general recommendations.

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

*Do not retreat until toxicity has recovered to ≤ grade 2, and 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

AST/ALT		**Bilirubin**	**Epirubicin (% previous)**	**Fluorouracil (% previous)**	**Cyclophosphamide (% previous)**
2-4 x ULN	Or	1-2 x ULN	50%	No change	No change
>4 X ULN	Or	2-4 X ULN	25%	No change	Caution
		> 4 X ULN	Discontinue	Discontinue	Caution

Renal Impairment

Creatinine Clearance (mL/min)	Cyclophosphamide (% previous dose)	Fluorouracil (% previous dose)	Epirubicin (% previous dose)
>30-50	100%	100%	
10-30	50-75%	Consider ↓ dose	
<10	50% or OMIT	↓ dose	

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F - Adverse Effects

Refer to fluorouracil, EPIrubicin, 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
• Nausea and vomiting • Cystitis • Myelosuppression ± infection, bleeding • Stomatitis and diarrhea • Alopecia • Anorexia, fatigue • Fever • ↑ LFTs • Rash, hand-foot syndrome, photosensitivity • Conjunctivitis	• Pneumonitis • SIADH, renal failure, VOD • DIC, hemolytic uremic syndrome, hemolysis • Secondary malignancies • Venous/arterial thromboembolism • Cardiotoxicity, AMI, arrhythmia • Rhabdomyolysis • Pancreatitis

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to fluorouracil, EPIrubicin, 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

- CBC; baseline and before each cycle
- Liver and renal function tests; baseline and before each cycle
- Cardiac examination especially with risk factors (including prior therapy with doxorubicin, mitoxantrone, or other cardiotoxic drug), or a cumulative epirubicin dose of > 900mg/m^2; baseline and as clinically indicated
- Clinical toxicity assessment (including GI, infection, cardiotoxicity, pulmonary, local toxicity, cystitis); 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	1.5 hours
Pharmacy Workload (average time per visit)	33.915 minutes
Nursing Workload (average time per visit)	61.667 minutes

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K - References

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

Keiling R, Armand PP, Hurteloup P, et al, French FAC vs. FEC study in advanced breast cancer. Onkologie, 1986; 9 (Suppl 1): 8-10.

French Epirubicin Study Group. A prospective randomized trial comparing epirubicin monochemotherapy to two fluorouracil, cyclosphosphamide and epirubicin regimens differing in epirubicin dose in advanced breast cancer patients. J Clin Oncol, 1991; 9: 305-312.

Periti P, Pannuti F, et al, Combination chemotherapy with cyclophosphamide, fluorouracil, and either epirubicin or mitoxantrone: A comparative randomized multicentre study in metastatic breast carcinoma. Cancer Invest, 1991; 9: 249-255.

Italian Multicentre Breast Study with Epirubicin. Phase III randomized study of fluorouracil, epirubicin, and cyclophosphamide v fluorouracil, doxorubicin, and cyclophosphamide in advanced breast cancer: An Italian multicentre trial. J Clin Oncol, 1988; 6: 976-982.

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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