Regimen Monograph

A - Regimen Name

EPIR Regimen

EPIrubicin

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

EPIrubicin	60-90 mg /m²	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or limited by cardiotoxicity risk/ unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

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.

Dosage with toxicity

Suggested dose levels: 90, 75, 50 mg/m^2

Worst Toxicity / Counts in Prior Cycle	Epirubicin Dose for Next Cycle
Febrile neutropenia / Thrombocytopenic bleeding / ANC grade 4 ≥ 7 days	↓ 1 dose level*
Cardiotoxicity**	Discontinue
Grade 3 related organ / non-hematologic	↓ 1 dose level*
Grade 4 related organ / non-hematologic	Discontinue

*Do not start new cycle until organ toxicity ≤ grade 2, platelets ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L

**including any signs and symptoms of heart failure, > 10% decline in LVEF to below the lower limit of normal, > 20% decline in LVEF from any level, or LVEF ≤ 45%.

Hepatic Impairment

Hepatic Impairment	% of Epirubicin recommended starting Dose
Bilirubin 21-51 micromol/L or AST 2-4 x ULN	50
Bilirubin > 51 micromol/L or AST > 4 x ULN	25
Severe	Use is contraindicated

Renal Impairment

Adjust dose with severe renal impairment (creatinine > 442 micromol/L).

Dosage in the Elderly

Use with caution; no adjustment required. Plasma clearance of epirubicin in female patients > 70 years of age was noted to be reduced by 35%.

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F - Adverse Effects

Refer to EPIrubicin drug monograph(s) for additional details of adverse effects

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 • Myelosuppression ± infection,	• Fatigue • Diarrhea	• Injection site reaction (may be severe) • Conjunctivitis / keratitis	• Cardiotoxicity • Secondary Leukemia • Arterial / venous thromboembolism

bleeding (may be severe) • Menopausal symptoms • Mucositis • Urine discolouration			• Radiation recall reaction • Hypersensitivity (may be severe) • GI hemorrhage • Hyperuricemia • Pneumonitis

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G - Interactions

Refer to EPIrubicin drug monograph(s) for additional details

- Avoid concomitant use with cimetidine and other drugs affecting hepatic metabolism.
- Patients treated with trastuzumab should avoid anthracycline-based therapy for up to 28 weeks after stopping trastuzumab.
- Caution if used in combination with taxanes. If concomitant use is warranted, administer epirubicin first and taxane at least 24 hours later.

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H - Drug Administration and Special Precautions

Refer to EPIrubicin drug monograph(s) for additional details

Administration

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline). Doses of 100-120mg/m^2 should be infused over 15-20 minutes. For lower dose volumes, the infusion time may be proportionally decreased to no less than 3-5 minutes.
- Do not admix with other drugs. Incompatible with heparin.
- Avoid contact with alkaline solutions since this can lead to hydrolysis of epirubicin.
- Slow down injection rate if erythematous streaking or facial flushing occurs.

- If any signs or symptoms of extravasation occur, the injection or infusion should be immediately terminated and restarted in another vein. Any known or suspected extravasation should be managed promptly as per local guidelines and should include application of ice to the affected area.

- Keep refrigerated (2-8^{o}C). Protect from light.

Contraindications

- Hypersensitivity to epirubicin, any components of the product, other anthracyclines or anthracenediones
- Severe myelosuppression induced by prior chemotherapy or radiotherapy
- Severe hepatic impairment
- Severe myocardial insufficiency
- Recent myocardial infarction
- Severe arrhythmias
- History of severe cardiac disease
- Previous treatment with maximum cumulative doses of anthracyclines or anthracenediones

Warnings/Precautions

- Avoid live vaccines; use may result in serious infections in immunocompromised patients.
- Patients who have received mediastinal radiotherapy, other anthracycline/ anthracenediones/ cardiotoxic drugs, pre-existing heart disease are at increased risk of cardiotoxicity.

Pregnancy/Lactation

- Epirubicin is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **6 months** (general recommendation) after the last dose.
- Breastfeeding is not recommended.
- Fertility effects: probable.

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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, before each cycle, and as clinically indicated
- Cardiac function tests (Echo, RNA and/or MUGA scans) for all patients with cardiac risk factors and cumulative doses > 650mg/m^2; Baseline and as clinically indicated
- Clinical toxicity assessment of GI effects, dermatologic effects, tumour lysis syndrome, infection, bleeding, ocular effects, cardiotoxicity, local toxicity; 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 hour

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K - References

Epirubicin drug monograph, Cancer Care Ontario.

Perez DJ, Harvey VJ, Robinson BA, et al. A Randomized Comparison of Single-Agent Doxorubicin and Epirubicin as First-Line Cytotoxic Therapy in Advanced Breast Cancer. J Clin Oncol (1991) 9:2148-2152.

Findlay BP, Walker-Dilks C. Epirubicin, alone or in combinationchemotherapy, for metastatic breast cancer. Provincial Breast Cancer Disease Site Group and Provincial Systemic Treatment Disease

Site Group. Cancer Prev Control 1998 Jun; 2(3): 140-146.

August 2019 Updated Adverse Effects, Dosing in Hepatic Impairment, Dosage in Elderly, Interactions, Drug Administration and Special Precautions and Monitoring sections

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L - Other Notes

- If Epirubicin is given at a lower dose q7 days, see regimen EPIR(W)

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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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