Systemic Anti Cancer Treatment Protocol

EC (Epirubicin Cyclophosphamide)
Adjuvant/Neo-adjuvant regimen

PROTOCOL REF: MPHAECANBR

(Version No: 1.0)

Approved for use in:

ER positive, HER2 negative ("Luminal A/B"):

For Adjuvant or Neo-adjuvant intent.

For fit but lower risk – node negative, intermediate risk oncotype or 1-3 node positive patients in whom the consultant wishes to avoid taxane;

EC x 6

Or

EC x 4 for lowest risk patients.

Triple negative breast cancer, adjuvant use:

Use EC x 6 (or EC x 4 if lower risk) if wish to avoid a taxane.

Dosage:

Drug	Dosage	Route	Frequency
Epirubicin	**90mg/m²**	**IV**	Every 21 days For 4 to 6 cycles
Cyclophosphamide	**600mg/m²**	**IV**	

Supportive treatments

Dexamethasone 4mg orally twice a day for three days

Ondansetron 8mg orally twice a day for three days

Domperidone 10mg tablets three times a day when required

Filgrastim subcutaneous injection daily for 7 days from day 3 (dose of 300 micrograms for patients below 70kg, and 480 micrograms for those 70kg and above)

Extravasation risk:

Epirubicin: vesicant. Erythematous streaking along the vein proximal to the site of injection has been reported, and must be differentiated from an extravasation event. This reaction usually subsides within 30 minutes.

Cyclophosphamide – neutral

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	**Ondansetron tablets** 30mins before chemotherapy	**24mg**	**PO**	
	Dexamethasone tablets 30mins before chemotherapy	**12mg**	**PO**	
	Epirubicin	**90mg/m^2**	**IV**	IV bolus over 10 to 15 minutes Concurrent administration, doxorubicin at 400mL/hr and sodium chloride 0.9% at 100mL/hr
	Cyclophosphamide	**600mg/m^2**	**IV**	IV bolus over 30 minutes

- Nasal stuffiness can occur immediately with administration of cyclophosphamide, if uncomfortable for the patient the drug can be slowed down
- Encourage an oral fluid intake of 2 litres per day to promote urinary output & prevent chemical cystitis with cyclophosphamide.

Main Toxicities:

Haematological	Neutropenia, thrombocytopenia and anaemia.
Gastrointestinal	Nausea, vomiting, stomatitis, diarrhoea, mucositis
Cardiotoxicity	Epirubicin - sinus tachycardia and/or electrocardiogram (ECG) abnormalities such as non-specific ST-T wave changes. Congestive heart failure. Other cardiac events have been reported, included delayed toxicity.
Dermatological	Alopecia, normally reversible, although can be permanent following docetaxel.
Urological	Red colouration of urine for 1 to 2 days after administration following epirubicin
Ocular	Watery eyes, gritty and irritated
Urological	Urotoxicity can occur with short-term and long-term use of cyclophosphamide. Hemorrhagic cystitis, pyelitis, ureteritis, and haematuria. Mesna can be given if required.
Infertility	Amenorrhea, risk of premature menopause However ensure appropriate contraceptive advice is given

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Comments
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	Every cycle
ECHO / ECG	X					If clinically indicated
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
Informed Consent	X					
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

ECHO/ECG at baseline if pre-existing cardiac risk factors

Dose Modifications and Toxicity Management:

Haematological Toxicity:

Proceed with treatment if;

Neutrophils $\geq$ 1.0 **and** platelets $\geq$ 100 x 10^9/L

Defer by 7 days or until blood counts recovered if neutrophils $\leq$ 1.0 **or** platelets $\leq$ 100 x 10^9/L

Second episode or severe febrile neutropenia: Defer by 7 days or until blood counts recovered if neutrophils $\leq$ 1.0 **or** platelets $\leq$ 100 x 10^9/L **and reduce** to 80% dose

Hepatic impairment:

	Epirubicin	Cyclophosphamide
Bilirubin µmol/L	**Dose**	**Dose**
24 to 50	50%	100%
51 to 85	25%	75%
Above 85	Omit	Omit

Renal impairment:

No dose adjustments required for moderate renal impairment.

References:

Smith JW et al

Epirubicin with cyclophosphamide followed by docetaxel with trastuzumab and bevacizumab as neoadjuvant therapy for HER2 positive locally advanced breast cancer NSABP FB-5

Clin Breast Cancer 2016 17(1)48-54

Jones, RL et al
A randomised pilot phase II study of AC or EC given 2 weekly with pegfilgrastim vs 3 weekly for women with early breast cancer
British Journal of Cancer 2009 100: 305-310

The Renal Drug Handbook 4th edition, Ashley C and Dunleavy A. Radcliffe Publishing. 2014