

**Systemic Anti Cancer Treatment Protocol**

**Epirubicin Cisplatin Capecitabine  
(ECX gastric)**

**PROTOCOL REF: MPHAUGIECX  
(Version No: 1.0)**

**Approved for use in:**

Gastric / gastro-oesophageal junction adenocarcinoma

Neoadjuvant

Adjuvant

Locally advanced / metastatic disease

**Dosage:**

<b>Drug</b>	<b>Dosage</b>	<b>Route</b>	<b>Frequency</b>
Epirubicin	50mg/m <sup>2</sup>	IV	Every 21 days
Cisplatin	60mg/m <sup>2</sup>	IV	Every 21 days
Capecitabine	625mg/m <sup>2</sup> BD	PO	Continuous

**Supportive treatments:**

**Antiemetic risk**

Dexamethasone 4mg orally twice a day for 3 days

Domperidone 10mg oral tablets, up to 3 times a day or as required

Loperamide 2mg after each loose stool

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### **Drug Interactions**

Phenytoin – potentially toxic levels of phenytoin have been reported- monitor carefully

Warfarin and other coumarin anticoagulants – increased bleeding risk, monitor INR carefully, consider switch to LMWH

Sorivudine and analogues – Potentially fatal interaction – avoid completely

Allopurinol – reduced efficacy of capecitabine – avoid

### **Extravasation risk:**

Epirubicin – vesicant – follow trust / network extravasation policy. Specific treatment available

Cisplatin – Irritant - Follow trust / network extravasation guidelines, no specific treatment needed

### **Administration:**

Review patient’s fluid intake over the previous 24 hours

Calculate creatinine clearance using Cockcroft and Gault equation

Day	Drug	Dosage	Route	Diluent and Rate
1	<b>Aprepitant</b> 30 minutes prior to chemotherapy	125mg	PO	With 80mg on days 2 and 3
1	<b>Dexamethasone</b> 30 minutes prior to chemotherapy	12mg	PO	
1	<b>Ondansetron</b> 30 minutes prior to chemotherapy	24mg	PO	
1	Furosemide	20mg	PO	
1	<b>Epirubicin</b>	<b>50mg/m<sup>2</sup></b>	IV	IV bolus with concurrent sodium chloride 0.9%
1	Sodium Chloride 0.9% with 20mmol potassium chloride	1000mL	IV	Over 90 minutes
1	Monitor urine output – see notes below			
1	<b>Cisplatin</b>	<b>60mg/m<sup>2</sup></b>	IV	1000mL Sodium Chloride 0.9% over 90 minutes

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	Sodium Chloride 0.9% with 20mmol potassium chloride	1000mL	IV	Over 90 minutes
1 to 21	<b>Capecitabine</b>	<b>625mg/m<sup>2</sup> BD</b>	PO	Morning and evening continuously

**Neo adjuvant:** Give 3 cycles

**Adjuvant** – Give 3 cycles post operatively

**Advanced** – Give 3 cycles and reassess, may continue to 6 cycles subject to patient choice, tolerability and response

### Notes

Ensure adequate hydration pre and post cisplatin

Do not start Cisplatin infusion unless urine output is at least 100mL/hour estimated from the previous 3 hours

If necessary administer further 500mL 0.9% sodium chloride and furosemide 20mg orally.

The patient should be asked to drink 2 litres of fluid over 24 hours after the infusion and should contact the unit immediately if unable to do so for any reason.

### Capecitabine

Caution in patients with pre-existing heart disease, angina pectoris, arrhythmias or taking high dose aspirin or coumarin anticoagulants

### Counselling points:

Tablets should be taken 12 hours apart, morning and evening

Swallow whole with water within 30 minutes of a meal

Do not add doses missed onto the end of the cycle. Continue according to the treatment plan and stop taking on the originally scheduled day.

Take missed doses if remembered within 2 hours of the normal scheduled time.

Otherwise continue with the next scheduled dose. Do not double up missed doses

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In case of swallowing difficulties the tablets may be dissolved in 200mL warm water (boiled and cooled). Once dissolved stir the contents with a spoon and drink immediately. Wash well and reserve the glass and spoon for chemotherapy administration only.

**If capecitabine cannot be administered then alternative regimen infusional fluorouracil is an alternative (ECF regimen)**

Day	Drug	Dosage	Route	Diluent and Rate
1	<b>Aprepitant</b> Immediately prior to hydration	125mg	PO	With 80mg on days 2 and 3
1	<b>Dexamethasone</b> Immediately prior to hydration	12mg	PO	
1	<b>Ondansetron</b> Immediately prior to hydration	24mg	PO	
1	Furosemide	20mg	PO	
1	<b>Epirubicin</b>	<b>50mg/m<sup>2</sup></b>	IV	IV bolus with concurrent sodium chloride 0.9%
1	20mmol potassium chloride	Sodium Chloride 0.9% 1000mL	IV	Over 90minutes
1	Monitor urine output – see notes below			
1	<b>Cisplatin</b>	<b>60mg/m<sup>2</sup></b>	IV	1000mL Sodium Chloride 0.9% over 90 minutes
	20mmol potassium chloride	Sodium Chloride 0.9% 1000mL	IV	Over 90 minutes
1 to 7	<b>Fluorouracil</b>	<b>200mg/m<sup>2</sup>/24hours</b>	IV	Continuous via infusor device over 7 days
8 to 14	<b>Fluorouracil</b>	<b>200mg/m<sup>2</sup>/24hours</b>	IV	Continuous via infusor device over 7 days
15 to 21	<b>Fluorouracil</b>	<b>200mg/m<sup>2</sup>/24hours</b>	IV	Continuous via infusor device over 7 days

## Main Toxicities:

Myelosuppression, alopecia, renal impairment, nausea and vomiting, stomatitis, ovarian failure/infertility, cardiotoxicity

Cisplatin: Neuropathy, ototoxicity, nephrotoxicity

Capecitabine / Fluorouracil: Diarrhoea, PPE

DPD deficiency – leads to severe early fluorouracil toxicity, affects approximately 3% of population, may be life threatening

## Investigations and treatment plan

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X	X	X	At end of treatment
Nursing Assessment	X	X	X	X	X	Every cycle
CT scan	X					Surgical arrangement if neoadjuvant intent
FBC	X	X	X	X	X	Every cycle
U&E, LFT, Mg2+	X	X	X	X	X	Every cycle
CrCl (Cockroft and Gault)	X	X	X	X	X	Every cycle
Informed Consent	X					
ECG	X					If clinically indicated
Blood pressure measurement	X					Repeat if clinically indicated
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

**For ECF regimen blood tests are not required on day 8 and day 15.**

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## Dose Modifications and Toxicity Management:

For patients with specific cisplatin related toxicities who are still fit to continue treatment e.g. tinnitus, consider switch to EOX.

### Haematological toxicity

Proceed on day 1 if:-

ANC $\geq 1.0 \times 10^9/L$	Platelets $\geq 75 \times 10^9/L$
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Delay 1 week on day 1 and dose reduce as per table below, if:-

ANC $\leq 0.9 \times 10^9/L$	Platelets $\leq 74 \times 10^9/L$
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Day 1 of cycle	Epirubicin dose	Cisplatin dose	Capecitabine dose
ANC 0.5 to $0.9 \times 10^9/L$ OR Platelets 50 to $74 \times 10^9/L$	75%	Full	Full
ANC $< 0.5 \times 10^9/L$ OR Platelets 25 to $49 \times 10^9/L$	50%	Full	Full
Platelets $< 25 \times 10^9/L$	Omit	Full	Full

### Non-haematological toxicity

<b>Renal</b>	Cisplatin is eliminated primarily (>90%) in the urine and is itself nephrotoxic. If there is any significant renal toxicity discuss with consultant before proceeding. Recalculate CrCl using Cockcroft and Gault every cycle		
	<b>GFR (mL/min)</b>	<b>Cisplatin dose</b>	<b>Capecitabine dose</b>
	$\geq 60$	100% dose	100% dose
	50 to 59	50% dose	100% dose
	40 to 49	50% dose	75% dose
	<40	Consider carboplatin	75% dose
<b>Hepatic</b>	If bilirubin increases to 1.5 times ULN epirubicin should be omitted until it returns to normal level.  If bilirubin increases to 3 times ULN or ALT/AST to 2.5 times ULN, omit capecitabine until liver function recovers  No modifications needed with cisplatin		

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**Capecitabine dose adjustment guidelines for non haematological toxicities, including diarrhoea, vomiting, stomatitis, and PPE**

<b>Common Toxicity Criteria</b>	<b>Dose changes within a treatment cycle</b>	<b>Dose adjustment for next cycle/dose (% of starting dose)</b>
Grade 1	Maintain dose level	Maintain dose level
<b>Grade 2</b>		
-1st appearance	Interrupt until resolved to grade 0-1	100%
-2nd appearance		75%
-3rd appearance		50%
-4th appearance	Discontinue treatment permanently	Not applicable
<b>Grade 3</b>		
-1st appearance	Interrupt until resolved to grade 0-1	75%
-2nd appearance		50%
-3rd appearance	Discontinue treatment permanently	Not applicable
<b>Grade 4</b>		
-1st appearance	Discontinue permanently Or If physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50% (consultant approval only)
-2nd appearance	Discontinue permanently	Not applicable

**Capecitabine**

<b>Diarrhoea</b>	Treat symptomatically with loperamide at standard doses, codeine may be added. If persistent or grade 3 or 4 stop capecitabine until resolved to grade 0 or 1. Restart as per CTC table above for dose reductions
<b>Stomatitis</b>	Regular mouthwashes (water, saline or non alcoholic proprietary brand), brush gently with a soft brush, adequate pain relief, nutritional support in severe cases – see above for dose reductions.
<b>PPE</b>	Manage as per trust policy, withhold treatment until resolved to grade 1, dose reductions as per CTC table above.
<b>Conjunctivitis</b>	Eye drops for symptomatic treatment
<b>Chest Pain / coronary artery spasm</b>	Stop capecitabine, standard angina investigations, refer to consultant, if symptoms persist stop capecitabine permanently

**References:**

Cunningham, D et al; NEJM 2008; 358: 36-46 (REAL-2)

Cunningham, D et al; NEJM 2006; 355: 11-20 (peri-operative ECF)

Wagner, A et al; JCO 2006; 24 (18) 2903 - 2909

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