ECX – Epirubicin, Cisplatin and Capecitabine

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Drug	Dose	Route	Diluent	Rate
Day 1	Sodium Chloride 0.9%	250 ml	Infusion	Fast Running	
	Furosemide	20 mg	IV bolus	Via saline drip	
	Mg SO4 KCl	10mmol 20mmol	Infusion	1000ml NaCl 0.9%	Over 2 hours
	Aprepitant	125mg	Oral		
	Dexamethasone	8 mg	Oral		
	Aprepitant	125mg	Oral		
	Ondansetron or Palonosetron	8mg or 250micrograms	Oral/Slow bolus/15 min infusion or IV bolus		
	Epirubicin	**50 mg/m^2**	**IV Bolus**		
	Cisplatin	**60 mg/m^2**	**IV Infusion**	1000ml NaCl 0.9%	Over 2 hours
	Mg SO4 KCl	10mmol 20mmol	Infusion	1000ml NaCl 0.9%	Over 2 hours
1 to 21	**Capecitabine**	**625 mg/m^2 TWICE DAILY**	Oral		

DOSE FORM
Capecitabine is supplied as 150mg and 500mg tablets, therefore calculated doses must be rounded to the nearest 150mg.

CYCLE LENGTH AND NUMBER OF DAYS
21 DAYS usually for 6-8 cycles

APPROVED INDICATIONS
Neoadjuvant/adjuvant/perioperative treatment of oesophago-gastric cancers

ELIGIBILITY CRITERIA
ECOG performance status 0-1, Karnofsky performance status >70%, adequate hepatic, renal, marrow and cardiac function

EXCLUSION CRITERIA
Inability to swallow Capecitabine tablets

PREMEDICATION
Adequate hydration and urinary flow is essential when administering cisplatin. Patients should be weighed (with bladder empty) prior to commencing treatment and to use 20 mg of IV Furosemide as a diuretic given routinely if there is no contraindication. Patient should be re-weighed at the end of cisplatin (with empty bladder) and consideration given to administering a further dose of Furosemide if weight gain is more than 1.5 Kg.

RECOMMENDED TAKE HOME MEDICATION

Aprepitant 80mg orally, on days 2 and 3
Ondansetron 8mgs twice daily for 2 to 3 days (not given if using palonosetron)
Dexamethasone 4mg twice daily for 1 to 3 days
Metoclopramide 10 mg three times daily as required
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED

FBC, U&Es and LFTs. Check renal function before commencing platinum. Use EDTA or Wright formulae to calculate GFR. GFR must be above 60ml/min for cisplatin-based treatment. If GFR <60ml/min discuss with an Oncology Specialist.

Prior to each cycle

FBC, U&Es, LFTs as required; GFR doubled checked using Wright formulae

ASSESSMENT OF RESPONSE

Metastatic: Tumour size and patient symptomatic response

REVIEW BY CLINICIAN

To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW

On cycles where not seen by clinician.

ADMINISTRATION NOTES

Counselling Points for Oral Capecitabine

How to take: Take tablets 12 hours apart, within 30 minutes after the end of meal (i.e. breakfast & evening meal.) Swallow whole with water

Side effects Common side effects to discuss with patient include; diarrhoea, nausea & vomiting, stomatitis (mouth ulcers), hand-foot syndrome (painful red swelling in hands and feet), fever or infection. If patients notice any of these advise them to stop taking treatment, contact doctor/chemotherapy day unit who will take steps to manage side effects and advise on continuing treatment.

*Missed dose***:** If remember half an hour after they should have taken their tablets, then take the missed dose, otherwise only take the regular dose at next scheduled time. Do not double-up doses to make up for the missed doses or take extra doses at the end of the treatment cycle.

Post dose vomiting: In the case of vomiting within a few hours after drug intake, never repeat the administration of the dose.

Storage/ Disposal Tablets should be stored in cool dry place less than 30°C. Unused medicines must be returned to hospital pharmacy for disposal

Diarrhoea is common and may require intervention with fluids and electrolytes if severe. If diarrhoea is a problem, give loperamide 2 to 4 mg four times daily as required or codeine phosphate 30mg four times daily and stop taking Capecitabine if diarrhoea moderate/severe.

EXTRAVASATION See NCA/ Local Policy

Epirubicin is a vesicant drug. If extravasation occurs there is high risk of tissue damage

TOXICITIES

- Palmar/Plantar Erythrodysesthesia - Can be severe, patients must be forewarned
- Myelosuppression
- Nephrotoxicity due to cisplatin
- Cardiotoxicity. Maximum cumulative dose of epirubicin 900 mg/m^2
- Nausea & Vomiting
- Diarrhoea
- Stomatitis
- Hyperpigmentation
- Alopecia
- Ototoxicity
- Neurotoxicity
- Metallic taste on administration
- Red urine for up to 24 hours with epirubicin
- Occasionally patients with heart disease may experience coronary artery spasm.

DOSE MODIFICATION / TREATMENT DELAYS

Haematological toxicity:
Delay 1 week if ANC < 1.0 or platelets < 75

ANC	PLT	Adjustment
≥ 1.0	≥ 75	Full dose
0.5 – 1.0	50 – 75	Interrupt capecitabine, delay carboplatin and epirubicin until recovery. Restart epirubicin with 25% dose reduction
< 0.5	25 - 50	Interrupt capecitabine and delay carboplatin and epirubicin until recovery. Restart epirubicin with 50% dose reduction

- Grade III infection associated with neutropenia requires a dose reduction of epirubicin by 25%
- Grade IV infection associated with neutropenia requires a dose reduction of epirubicin by 50%

Non-Haematological Toxicity for Oral Capecitabine
Any patient with CTC toxicity should be prescribed the therapeutic option for grade 1 toxicity in addition to dose modification.

Table of hand/ foot toxicity grading for capecitabine only

Grade	Clinical	Functional
1	Numbness, dysesthesia/paraesthesia,	Discomfort but no interruption Of normal activities
2	Painful erythema with swelling	Discomfort which affects activities of daily living
3	Moist desquamation, ulceration, blistering, severe pain	Severe discomfort, unable to work or perform activities of daily living

Table of Diarrhoea toxicity grading for capecitabine only

CTC Grade	Toxicity	% Capecitabine
1	Diarrhoea (watery stool 2-3 times/day)	Hold until recovery, then resume at 100% dose for remainder of course
2	Diarrhoea (watery stool 4-6 times/day)	Hold until recovery, then resume at 75% dose for remainder of course
3/4	Diarrhoea (watery stool >7 times/day	Following grade 3 or 4 diarrhoea, subsequent doses of capecitabine should be decreased or treatment discontinued permanently (grade 4).

Table of dose adjustments according to CTC toxicity

	Grade 2	Grade 3	Grade 4
1st appearance	Interrupt until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible	Interrupt until resolved to grade 0/1, then continue at 75% of original dose with prophylaxis where possible	**Discontinue treatment**
2nd appearance	Interrupt until resolved to grade 0/1, then continue at 75% of original dose	Interrupt until resolved to grade0/1, then continue at 50% of original dose	
3rd appearance	Interrupt until resolved to grade 0/1, then continue at 50% of original dose	**Discontinue treatment**	
4th appearance	**Discontinue treatment**		

Renal dysfunction:

Capecitabine

- Capecitabine is renally excreted; therefore, patients with moderate renal impairment (CrCl < 50ml/min) require a 25% dose reduction.
- Contra-indicated in severe renal failure (CrCl < 30ml/min) (Wright equation or measured GFR)

Cisplatin

- Baseline EDTA required. GFR prior to treatment should be >60mls/min
- Serum creatinine should be checked before each cycle of treatment. If there is a >20% increase compared to the baseline, then the EDTA must be repeated.
- If renal function deteriorates the Cisplatin dose must be adjusted as follows

GFR (EDTA or measured Creatinine Clearance)	Cisplatin Dose
60ml/min	Full dose
40-59ml/min	Consider giving same cisplatin dose in mg as value of GFR in ml/min
< 40ml/min	Omit cisplatin. Consider substituting for Carboplatin AUC 3-5

Conversely if a patient has a GFR < 60mls/min initially and there is improvement in serum creatinine the GFR should be rechecked with an EDTA clearance.

Hepatic dysfunction:

- If bilirubin > 24µmol/L, then epirubicin should be omitted
- No studies have been performed to examine safety of capecitabine in severe hepatic dysfunction.
- IF ALT > 5ULN or ALP > 5ULN, DO NOT GIVE and consult with prescriber before proceeding

Patients with functional hearing loss should have cisplatin omitted. Carboplatin AUC 3-5 can be substituted but must be authorised by the SpR/Consultant. The reason & the change must be clearly documented in the patient's notes

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCES:

1. Findlay M et al. A Phase II study in advanced gastric cancer using epirubicin and cisplatin in combination with continuous 5-FU (ECF). Ann Oncol 1994; 5:609-616.
2. Cunningham D et al. Capecitabine and Oxaliplatin for Advanced Esophago - gastricancer. NEJM 2008 358;1:36-46

Document Control

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Summary of Changes	1.1	Reformatted from old NCN/CCA versions	
	1.2	Protocol reviewed. Typing errors corrected. Epirubicin cumulative dose amended. Epirubicin and Cisplatin in renal/hepatic impairment advice added	
	1.3	Protocol reviewed and reissued, Antiemetic advice updated	
	1.4	Updated against Chemocare protocol, parameters, antiemetics.	